Exhibit C

A MEDWATCH CONTINUING EDUCATION ARTICLE

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THE CLINICAL IMPACT OF ADVERSE EVENT REPORTING

Learning Objectives:

Upon completion of this program, health professionals should be able to:

- Identify underlying principles of postmarketing surveillance
- Understand reporting requirements (health professionals, manufacturers, user facilities) regarding regulated medical product safety
- Discuss basic limitations/strengths of data derived from postmarketing surveillance
- List examples of FDA regulatory actions that have been based on postmarketing surveillance
- Describe how FDA disseminates information regarding medical product safety
- Understand how a national postmarketing surveillance program impacts clinical practice

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Nomifensine (Merital®), an antidepressant that had been available in Germany since 1976, had been prescribed to an estimated ten million patients prior to its marketing in the U.S. in July, 1985[1,2]. Initial labeling for the product reflected a variety of long-recognized hypersensitivity reactions, including fever, liver injury, hemolytic anemia and eosinophilia, that were apparently all readily reversible[3].

At the time of U.S. approval, FDA was aware of reports of less than twenty hemolytic anemia cases, all non-fatal; however, in 1985, when foreign adverse reaction reports showed the hemolytic anemia might be fatal, labeling was revised to reflect the potential seriousness of the reaction[3]. Due to an increase in serious hemolytic anemia cases seen in Europe, marketing of nomifensine was reconsidered by the manufacturer, who announced a worldwide withdrawal of the drug on January 21, 1986[3,4].

The case of nomifensine illustrates that the safety profile of a drug evolves over its lifetime on the market. Even after almost ten years experience, or longer, new information that will impact the clinical use of a medical product can be detected. Consequently, all medical products need to be continually assessed for safety within the context of their perceived benefit.

Medical product safety monitoring is an ongoing process accomplished through **Postmarketing Surveillance**, the collection of data about drugs [or any other medical product] once they are marketed and thus available to the general population[5]. This process encompasses adverse event reports evaluation, generation of safety-related hypotheses and use of techniques to evaluate these hypotheses.

THE NEED FOR POST-MARKETING SURVEILLANCE

While the U.S. has one of the most rigorous approval processes in the world, it is not possible to detect all potential problems during premarketing clinical trials. Medical product studies, ranging from preclinical animal testing and medical device bench testing to final tests in humans, have inherent limitations no matter how well they are designed or conducted. The need for postmarketing surveillance is a direct result of these limitations.

Premarketing Animal Studies

Most medical products are first tested in animals prior to introduction into humans. Animal studies have limitations in their ability to predict human toxicity; this is demonstrated by the case of practolol, a β_1-adrenoreceptor blocking agent withdrawn from the U.K. market in 1976 after several years of widespread use[6,7], and never marketed in the U.S.

The U.K. action was prompted by the serious adverse reactions of dermatitis, keratoconjunctivitis and sclerosing peritonitis, collectively termed the oculomucocutaneous syndrome[6,7]. This syndrome had not been seen during extensive preclinical animal testing conducted within required guidelines[7].

Subsequent toxicity studies in several small animal species (both those that metabolize practolol similarly to humans and those whose practolol metabolism is more extensive than humans) found no animal model for the observed human adverse reactions[8]. The lack of reproduction of these particular adverse reactions in any laboratory animal species[9] demonstrates that animal studies, no matter how appropriate or well-performed, are not necessarily predictive of human pathology.

Premarketing Human Clinical Studies

There are intrinsic limitations to premarketing human clinical trials with respect to their ability to detect adverse events. Short duration, narrow population, narrow set of indications and small size are major factors in this regard[10], irrespective of the type of medical product being studied.

The capability of premarketing clinical trials to discover rare adverse events is

particularly affected by their size. In order to have a 95% chance of detecting an adverse event with an incidence of 1 per 1,000, 3,000 patients at risk are required[11]; with no more than 3,000 to 4,000 individuals usually exposed to a medical product prior to marketing, only those adverse events with approximately 1/1,000 or greater incidence can be expected to be found.

While medical products are usually studied for several years before they are marketed, an individual patient in a clinical trial is generally exposed to the product for less than a year. Even long-duration premarketing clinical trials, which can last several years, do not provide the degree of patient exposure that will occur postmarketing with a chronically used medical product. In addition, the relatively short durations of clinical trials mitigate against the detection of adverse events with long latency.

Because of these limitations, premarketing clinical trials seldom detect or define the frequency of all important adverse events. As a result, the official labeling/product information at the time of approval of a medical product reflects what is known about that product's risk at that point in time. The controlled environment under which clinical trials are conducted means that the safety data presented in the original labeling of a product usually represents actual occurrence rates in the defined population that has been studied.

Postmarketing Experience

Health professionals should be aware that this is **not** the case with postmarketing data. Once a product leaves the controlled study environment and enters general clinical use, the ability to detect the actual incidence of an adverse event can essentially be lost. On the other hand, once a new product is marketed, there are great increases in the number and variety of patients exposed, including those with multiple medical problems and undergoing treatment with numerous concomitant medical products.

As a result, the population experience with the product will be much broader than that derived from the clinical trials. One particular safety-related advantage this offers is a generally greater capability to detect adverse events possibly related to interactions with other medical products than is available in the premarketing phase.

The major changes in the size and nature of the exposed patient population that occur once a medical product is available for widespread use emphasize the great importance of adverse event detection and reporting by health professionals.

MEDWATCH

It is with these considerations in mind that MEDWATCH, the FDA Medical Products Reporting Program, was established[12]. While FDA's longstanding postmarketing surveillance programs predate MEDWATCH, this educational/promotional initiative was designed to emphasize the responsibity of healthcare providers to identify and report adverse events related to the use of medical products. Through the MEDWATCH program health professionals can report serious adverse events and product problems that occur with such medical products as drugs, biologics, medical and radiation-emitting devices, and special nutritional products (e.g., medical foods, dietary supplements and infant formulas).

Causality is **not** a prerequisite for MEDWATCH reporting; **suspicion** that a medical product may be related to a serious event is sufficient reason for a health professional to submit a MEDWATCH report. However, a report on every adverse event is **not** sought - what is desired is an increase in the reporting of **serious** events. In that regard, TABLE 1 offers a guideline for adverse event reporting. However, health professionals are welcome to report any adverse event that they judge to be clinically significant.

TABLE 1 MEDWATCH
What is a Serious Event?

Any event that is

- Fatal
- Life-threatening
- Permanently/significantly disabling
- Requires or prolongs hospitalization
- Cogenital anomaly
- Requires intervention to prevent *permanent* impairment or damage

CLINICAL SYNOPSIS 1

BIOLOGICS

Intravenous Immunoglobulin and Aseptic Meningitis Syndrome

In early 1994, FDA learned of a report from the National Institutes of Health (NIH), which described a high rate of aseptic meningitis syndrome (AMS) occurring in patients being treated for neuromuscular diseases with high doses of intravenous immunoglobulin (IGIV). The patients had been receiving doses of 2 g/kg of IGIV, which is five to ten times higher than the normally recommended dosage. Six of 54 patients developed severe headache, meningismus, and fever within 24 hours of dosing. Cerebrospinal fluid (CSF) was consistent with AMS in four of the six.

Following this lead, 22 cases of IGIV-associated AMS which had been reported to the FDA were reviewed. Symptoms included fever and photophobia, and prominent painful headache. Twenty of the cases were associated with positive CSF findings, including leukocytosis (predominantly neutrophilic) and elevated protein.

Unexpectedly, 19 of the reports indicated that normal doses of IGIV had been administered (0.2 - 0.4 g/kg). The patients had been treated by withdrawal of the medication and administration of analgesics. Of particular note was the characteristic time course of IGIV-associated AMS. The illnesses all began between 12 and 24 hours after administration, and recovery ensued within several days following withdrawal of the medication.

As a result of this work, FDA and NIH workers published two articles on IGIV-AMS simultaneously in the same journal[45,46]. The FDA also directed IGIV manufacturers to modify labeling to include a Precaution statement about the occurrence of the syndrome.

POSTMARKETING REPORTING OF ADVERSE EVENTS

The FDA has the regulatory responsibility for ensuring the safety of all marketed medical products. Health professionals are critical to this process, in that the first hint of a potential problem originates with

the perceptive clinician who then reports the case to the appropriate source. It is important for all health professionals to be aware that some reporting is mandated by federal law and regulation while other reporting, although considered vital, is strictly voluntary.

By Health Professionals

Any postmarketing surveillance program depends on health professionals to report serious adverse events observed in the course of their everyday clinical work. Except for adverse events associated with specified vaccines, reporting by an individual health professional is voluntary.

Given the clinical importance of postmarketing surveillance, all healthcare providers (physicians, pharmacists, nurses, dentists and others) should look upon adverse event reporting as part of their professional responsibility. The American Medical Association[13] and American Dental Association[14] advocate (respectively) physician and dentist participation in adverse event reporting systems as an obligation[13,14]. Further, The *Journal of the American Medical Association* instructs its authors that adverse drug or device reactions should be reported to the appropriate government agency, in addition to submitting such information for publication[15].

Health professionals can use the voluntary MEDWATCH form to report adverse events or product problems related to any medical product, with the exception of those occurring with vaccines. Reports can be sent to FDA either directly or, in most cases, via the manufacturer.

Reports concerning vaccines should be sent to the Vaccine Adverse Event Reporting System (VAERS), a joint program of the FDA and the Centers for Disease Control and Prevention[16]. Certain events following immunization (e.g., paralytic poliomyelitis after oral poliovirus vaccine)[17] are mandated by the National Childhood Vaccine Injury Act of 1986 to be reported, but VAERS accepts all reports of suspected significant adverse events after any vaccine administration[16]. For more information on VAERS, call 1-800-822-7967.

Health professionals working in a hospital or other **user facility** (nursing home, ambulatory surgical facility, outpatient treatment facility and outpatient diagnostic facility) should be aware of the legal requirements for medical device-related reporting by user facilities mandated by the Safe Medical Devices Act of 1990 (SMDA) (see TABLE 2[18]). Under the SMDA, physicians' offices are excluded from the user facility definition and thus exempt from mandatory reporting requirements. The FDA likewise excludes other groups that perform similar functions to physicians' offices (e.g, dentists, optometrists, nurse practitioners) from mandatory reporting[18]. However, health professionals within a user facility should familiarize themselves with their institution's procedures for device-related reporting, and actively participate in the program.

TABLE 2

Medical Device Reporting (MDR) Requirements[18]

NB: days refers to working days, unless otherwise specified

- ***User Facility:***
  - **Deaths** (to FDA and manufacturer within 10 days)
  - **Serious injuries/illnesses** (to manufacturer within 10 days; to FDA if manufacturer unknown, also within 10 days)
  - **Semiannual Reports** (to FDA) of all reports sent to FDA and/or manufacturer (due January 1 and July 1)
- ***Manufacturer:***
  - **Deaths, serious injuries, malfunctions** (to FDA within 30 calendar days of becoming aware of event)
  - **"5-day Report"** [to FDA if become aware of 1) event(s) necessitating "remedial action to prevent an unreasonable risk of substantial harm to the public health" or 2) reportable event for which FDA has requested 5-day report]
  - **Annual Certification** of number of reports
- ***Distributor:***
  - **Deaths** (to FDA and manufacturer within10 days)
  - **Serious injuries/illnesses** (to FDA and manufacturer within 10 days)
  - **Malfunctions** (to FDA and manufacturer within 10 days)

Confidentiality: The FDA acknowledges that health professionals have concerns regarding their confidentiality as reporters, and that of the patients whose cases they report. In order to encourage reporting of adverse events, FDA regulations offer substantial protection against disclosure of the identities of both reporters and patients. This was further strengthened on July 3, 1995, when a regulation went into effect extending this protection against disclosure by preempting state discovery laws regarding voluntary reports held by pharmaceutical, biological and medical device manufacturers[19].

By Hospitals

The FDA, recognizing the valuable role that hospitals play in the detection of adverse events and problems with medical products, views every active hospital monitoring program as a vital component of the national postmarketing surveillance system. Hospital reporting of adverse events, both within and outside an individual facility, is a mixture of voluntary and mandatory reporting.

Adverse event monitoring by hospitals is linked to Joint Commission on Accreditation of Healthcare Organizations (JCAHO) standards. In order to be accredited, JCAHO requires each hospital to monitor for adverse events involving pharmaceuticals and devices, with medication monitoring to be a continual collaborative function[20]. JCAHO standards indicate that medical product adverse event reporting should be done per applicable law/regulation, including those of state/federal regulatory bodies[20].

The American Society of Health-System Pharmacists (ASHP) has also been instrumental in the evolution of active internal hospital adverse drug event (ADE)-monitoring systems. ASHP guidelines include delineated criteria for classifying an adverse drug reaction (ADR) as significant[21], unlike JCAHO standards, which do not mandate a specific definition for a serious ADE. ASHP guidelines specifically state serious or unexpected ADRs should be reported to FDA, manufacturer, or both[21].

As user facilities, hospitals are sub-

ject to mandatory federal medical device adverse event reporting. TABLE 2 (on previous page) outlines these requirements, which include reporting by the facility of suspected medical device-related deaths to both FDA and the manufacturer, and serious injuries/illnesses to the manufacturer or to FDA, if the manufacturer is unknown[18]. However, there are no federal laws or regulations that require hospitals to report pharmaceutical-related adverse events to the FDA, although they are strongly encouraged to do so regarding those events deemed serious.

Reporting Required By Law or Regulation

Reporting by individual healthcare providers is essentially voluntary. However, manufacturers and distributors of FDA approved pharmaceuticals (drugs and biologics) and medical devices, plus pharmaceutical packers and device user facilities, all have mandatory reporting requirements.

TABLE 3

Adverse Event (AE) Reporting Requirements for Pharmaceuticals[22,23]

- **15-day "Alert Reports":** each AE both serious and unexpected (i.e, not in the product's current labeling) must be reported to the FDA within 15 working days
- **Periodic AE Reports:** all non-15 day AE reports must be reported periodically (quarterly for the first three years after approval, then annually)
- **Other:** the frequency of reports of 1) AEs that are both serious and expected, and 2) therapeutic failures must be periodically monitored, and any significant increase must be reported within 15 days
- **Scientific Literature:** a 15-day report based on scientific literature (case reports; results from a formal clinical trial; epidemiology-based studies or "analyses of experience in a monitored series of patients")
- **Postmarketing Studies:** no requirement for a 15-day report on an AE acquired from a postmarketing study unless manufacturer concludes pharmaceutical causation for AE "reasonable possibility"

TABLE 3 outlines mandatory reporting regarding pharmaceuticals[22,23]. By regulation, these companies are required to report **all** adverse events of which they are aware to the FDA and to provide as complete information as possible. As can be seen, mandated pharmaceutical reporting relies heavily on information provided by health professionals through both voluntary reporting and the scientific literature.

In the case of over-the-counter (OTC) drugs, reports are only required on OTC products marketed under an approved New Drug Application (NDA), including those prescription drugs that undergo a switch to OTC status. Reports are **not** required for other OTC drugs (i.e., older drug ingredients which are marketed without an NDA), although voluntary reporting is encouraged.

Both prescription and OTC drugs require FDA safety and efficacy review

CLINICAL SYNOPSIS 2

MEDICAL DEVICES

Barium Enema Kits and Sudden Death

Three reports of sudden death associated with the use of barium enema kits were reported to the FDA. The first case, reported in 1989, involved a 49 year-old female with a history of atopic dermatitis, allergic rhinitis and asthma who was undergoing a barium enema for occult blood in her stool when she reported the onset of an allergic reaction[47]. The study was immediately terminated, but within minutes she began to have increasing dyspnea, then became cyanotic. The patient was intubated, and underwent unsuccessful resuscitation efforts[47].

In April 1990, two more cases of sudden death associated with the use of barium enema kits were reported. A 41 year-old female complained of nausea shortly after insertion and inflation of the tip/cuff assembly, went into cardiac arrest within 30 seconds and underwent unsuccessful resuscitation efforts. In the third case, a 72 year-old female had an immediate reaction after the tip portion of the tip/cuff assembly was inserted prior to introduction of the barium contrast agent, went into vascular collapse and died.

Review of the adverse event database revealed no other reports of reactions to barium enema procedures. However, literature review showed a potential problem with reactions to devices containing latex[48], of which the barium enema cuffs are made. Various FDA investigations were undertaken, including collection of samples of gloves, devices and lubricants.

As a result, the manufacturer of the enema tips voluntarily agreed to send out an urgent Medical Alert to approximately 10,000 radiologists that notified them of adverse reactions possibly associated with latex allergy that could occur during barium enema procedures. Minimizing use of tips with retention cuffs was requested, as was the use of non-cuffed tips whenever possible. Physicians were urged to screen patients for latex allergy histories and concomitant drug use.

Further regulatory actions were subsequently taken:

1) Health Hazard Evaluation of the tips/cuffs lead to the recommendation that the Medical Alert be expanded to include more health professionals and organizations. The firm added an additional washing of the cuffs in the manufacturing process and wrote a letter to all health professionals concerning allergic reactions associated with the use of barium enema products with latex cuffs;

2) After a second Health Hazard Evaluation determined that the problems associated with these devices presented a high risk of serious adverse health consequences, the firm initiated a recall of all latex cuffed enema tips;

3) An ad hoc FDA committee that was formed to consider additional action developed an FDA Medical Alert which outlined the occurrence of several severe allergic reactions to medical devices containing latex and suggested ways to screen and protect allergic patients. This was sent to approximately 1,000 radiological and medical organizations, and was published in the July 1991 *FDA Medical Bulletin*;

4) Manufacturers of latex devices received an FDA letter discussing how to manufacture latex products in order to minimize the possibility that latex contaminants are either a source of, or contributing factor to, adverse reactions to various types of latex devices.

These events led to a 1992 International Conference on latex sensitivity and the practice of physicians testing patients for latex sensitivity prior to undergoing surgical procedures.

prior to marketing, unlike dietary supplements (which include vitamins, minerals, amino acids, botanicals and other substances used to increase total dietary intake). By law[24] the manufacturers of dietary supplements do not have to prove safety or efficacy, so the onus is on the FDA to prove that a particular product is unsafe. As a result, direct-to-FDA voluntary health professional reporting of serious adverse events possibly associated with dietary supplements is particularly important.

TABLE 2 (on page 3) lists the medical device-related reporting required of user facilities, manufacturers, and distributors[18].

All unsolicited reports from health professionals received by FDA via either the voluntary or mandatory route are called **spontaneous** reports. A spontaneous report is a clinical observation that originates outside of a formal study[25]. The combination of adverse event information generated by **all** reporting makes up the database upon which postmarketing surveillance depends.

LIMITATIONS & STRENGTHS OF SPONTANEOUS REPORTS DATA

As with clinical trials, there are important limitations to consider when using spontaneously reported adverse event information. These limitations include difficulties with adverse event recognition, underreporting, biases, estimation of population exposure and report quality.

LIMITATIONS

Adverse Event Recognition

The recognition of ADEs [or any other medical product-associated adverse event] is quite subjective and imprecise[26]. While an attribution between the medical product and the observed event is assumed with all spontaneously reported events, every effort is made to rule out other explanations for the event in question. It is well known that placebos[27] and even no treatment[28] can be associated with adverse events. In addition, there is almost always an underlying background rate for any clinical event in a population, regardless of whether there was exposure to a medical product.

Reaching a firm conclusion about the relationship between exposure to a medical product and the occurrence of an adverse event can be difficult. In one study, clinical pharmacologists and treating physicians showed complete agreement less than half the time when determining whether medication, alcohol or "recreational" drug use had caused hospitalization[29].

Such considerations emphasize the crucial need for careful, thoughtful review of adverse event reports upon their receipt by FDA or the manufacturer. It is through this process that causality, or at least a high degree of suspicion for a product-adverse event association, is put to the test.

Underreporting

Another major concern with any spontaneous reporting system is underreporting of adverse events[16,30-32]. It has been estimated that rarely more than 10% of serious ADRs, and 2-4% of non-serious reactions, are reported to the British spontaneous reporting program[30]. A similar estimate is that the FDA receives by direct report less than 1% of suspected serious ADRs[32]. This means that cases spontaneously reported to any surveillance program, which comprise the **numerator**, generally represent only a small portion of the number that have actually occurred. The effect of underreporting can be somewhat lessened if submitted reports, irrespective of number, are of high quality.

Biases

Unlike clinical trial data, which are obtained under strictly controlled conditions, spontaneously reported information is uncontrolled, and therefore subject to the possible influence of a number of biases that can affect reporting. These biases include the length of time a product has been on the market, country, reporting environment, detailing time and quality of the data[33]. A striking illustration of the impact one such factor can have is the finding that the peak of spontaneous ADR reporting for a drug is at the end of the second year of marketing, with a subsequent precipitous decline in reporting[34] despite a lack of apparent decline in usage or change in ADR incidence[34,33]. In addition to these biases, it is possible that reported cases might differ from nonreported cases in characteristics such as time to onset or severity[35].

Estimation of Population Exposure

Compounding these numerator limitations is the lack of **denominator** data, such as user population and drug exposure patterns[35], that would provide the exact number of patients exposed to the medical product, and thus at risk for the adverse event of interest. Numerator and denominator limitations make incidence rates computed from spontaneously reported data problematic[35], if not completely baseless. However, even if the exposed patient population is not precisely known, estimation of the exposure can be attempted through the use of drug utilization data[36].

This approach, whose basic methodologies are applicable to medical products in general, can be of great utility. Major sources of data on the use of drugs by a defined population include market surveys based on sales or prescription data, third-party payers or health maintenance organizations, institutional/ambulatory settings or specific pharmacoepidemiological studies[36]. Cooperative agreements and contracts with outside researchers enable FDA to utilize such databases in its investigations. Device utilization studies employ the same sources of data, as well as Medicare-derived information.

Care must be taken in interpreting results from studies utilizing these databases. That drug prescribing does not necessarily equal drug usage[36], and the applicability of results derived from a specific population (such as Medicaid recipients) to the population at large, need to be weighed carefully.

Report Quality

The ability to assess, analyze and act on safety issues based on spontaneous reporting is dependent on the quality of information submitted by health professionals in their reports. A complete adverse event report should include the following: product name (and information such as model and serial numbers in the case of medical devices); demographic data; succinct clinical description of adverse event, including confirmatory/relevant test/laboratory results; confounding factors (such as concomitant medical products and medical history); temporal

information, including date of event onset and start/stop dates for use of medical product; dose/frequency of use (as applicable); biopsy/autopsy results (as applicable); dechallenge/rechallenge information (if available); and outcome.

Given the limitations of spontaneously reported data, what are its strengths?

STRENGTHS

Large-Scale and Cost-Effective

Two vital advantages of surveillance systems based on spontaneous reports are that they potentially maintain ongoing surveillance of all patients, and are relatively inexpensive[37]. In fact, they are probably the most cost-effective way to detect rare, serious adverse events not discovered during clinical trials.

Generation of Hypotheses and Signals

Making the best possible use of the data obtained through monitoring underlies postmarketing surveillance[38]. Towards that goal, the great utility of spontaneous reports lies in **hypothesis generation**[31], with need to explore possible explanations for the adverse event in question. By fostering suspicions[39], spontaneous report-based surveillance programs perform an important function, which is to generate **signals** of potential problems that warrant further investigation.

Assessment of the medical product-adverse event relationship for a particular report or series of reports can be quite difficult. TABLE 4 lists factors that are helpful in evaluating the strength of association between a drug and a reported adverse event[40].

TABLE 4

Useful Factors For Assessing Causal Relationship Between Drug and Reported Adverse Event[40]

- Chronology of administration of agent, including beginning and ending of treatment and adverse event onset
- Course of adverse event when suspected agent stopped **[dechallenge]** or continued
- Etiologic roles of agents and diseases in regard to adverse event
- Response to readministration **[rechallenge]** of agent
- Laboratory test results
- Previously known toxicity of agent

CLINICAL SYNOPSIS 3

SPECIAL NUTRITIONALS

L-tryptophan Related Eosinophilia-Myalgia Syndrome[49]

In July 1989, a healthy 44 year-old woman in Santa Fe with a history of allergic rhinitis started taking L-tryptophan, an essential amino acid available as an dietary supplement, for insomnia. By early September she was reporting onset of cough, shortness of breath and weakness. When first seen by a physician in late September, she presented with a puffy, flushed face, abdominal pain, mucosal ulcers, myalgia and weakness. Her white blood cell (WBC) count was 11,900 cells/mm^3, with an eosinophil count of 42%. Her condition worsened through October, with her WBC rising to 18,200 and eosinophil count to 45%.

Her physician consulted with a rheumatologist, who while not knowing what was wrong with this patient, did know of a second patient who had been hospitalized in Santa Fe with similar symptoms and eosinophil count. In mid-October, a third patient in New Mexico, who had an eosinophil count of 9,000 and had also been taking L-tryptophan, was discovered. While one patient was unusual and two was suspicious, three made it a cluster of a very uncommon disease.

All three original patients were middle-aged women. Although the severity differed, all had the common features of myalgia, weakness, oral ulcers, abdominal pain, shortness of breath and skin rash. While the doses of L-tryptophan they had used were similar, the duration of use prior to onset of illness varied from a few weeks to 2 years. Common laboratory features included striking leukocytosis, eosinophilia, elevated aldolase [with a normal creatine kinase (CK)] and abnormal liver function tests.

An article about the condition appeared in the November 7 *Albuquerque Journal News*. On November 11, FDA issued a Public Advisory against the use of L-tryptophan, followed four days later by the Centers for Disease Control and Prevention (CDC) establishment of a system of national state-based surveillance for the newly named eosinophilia-myalgia syndrome (EMS)[49].

On November 17, FDA requested a nationwide recall of all over-the-counter dietary supplements in capsule or tablet form providing 100 mg or more of L-tryptophan in a daily dose. On March 23, 1990, because of the identification of one case of EMS associated with a dietary supplement containing less than 100 mg, and continued efforts by some firms to circumvent the recall, the agency requested an expansion of the recall to all marketed products containing added manufactured L-tryptophan. Excepted were those that were permitted to contain added L-tryptophan under existing food additive regulations. Additionally, on March 22, the agency had imposed an import alert to detain all foreign shipments of manufactured L-tryptophan.

Because virtually all manufactured L-tryptophan is imported into the U.S., the practical effect of the recall and import alert was to effectively eliminate the availability of L-tryptophan-containing dietary supplements. Eventually, more than 1,500 cases of EMS, including 38 deaths, have been reported to the CDC, although the true incidence of the disorder is thought to be much higher.

The recognition of a cluster of cases was the key to the detecting of EMS. Interactions among various specialists, including a family physician, hematologist, rheumatologist, clinical immunologist and epidemiologists, was crucial to this process[49].

Of equal importance is ongoing basic and clinical research to explain the etiology and pathogenesis of this disorder. Although it is widely believed that contaminants or impurities in the L-tryptophan are responsible for EMS, continuing research indicates a role for "pure" tryptophan itself[50-52], as well as for certain host factors in the etiology of the disorder[53,54]. These findings support suggestions that the L-tryptophan-associated EMS was caused by several factors and is not necessarily related to a contaminant in a single source of L-tryptophan.

FDA concerns about the safety of L-tryptophan-containing products and the possibility of potential new cases of L-tryptophan-related EMS are underscored by recent information indicating the availability of L-tryptophan by American sources. Both EMS's clinical seriousness, and uncertainties surrounding its etiology, indicate the need for health professionals to remain vigilant regarding adverse events possibly associated with the use of L-tryptophan-containing dietary supplements, and to report such events to MEDWATCH.

The stronger the drug-event relationship in each case and the lower the incidence of the adverse event occurring spontaneously, the fewer case reports are needed to perceive causality[41]. It has been found that for rare events, coincidental drug-event associations are so unlikely that they merit little concern, with greater than three reports constituting a signal requiring further study[35]. In fact, it has been suggested that a temporal relationship between medical product and adverse event, coupled with positive dechallenge and rechallenge, can make isolated reports conclusive as to a product-event association[42]. Biological plausibility and reasonable strength of association aid in deeming any association as causal[30].

However, achieving certain proof of causality through postmarketing surveillance is unusual[41]. Attaining a prominent degree of suspicion is much more likely, and may be considered a sufficient basis for regulatory decisions[41].

Clinician Contribution

The reliance of postmarketing surveillance systems on health professional reporting enables an individual to help improve public health. This is demonstrated by one study that found direct practitioner participation in the FDA spontaneous reporting system was the most effective source of new ADR reports that led to changes in labeling[43]. Ensuring that the information provided in the adverse event report is as complete and in depth as possible further enhances postmarketing surveillance.

Thus, while possessing inherent limitations, postmarketing surveillance based on spontaneous reports data is a powerful tool for detecting adverse event signals of direct clinical impact. It is dependent not only on health professional participation, but also on the quality of the reports that are submitted.

FDA EVALUATION OF REPORTS OF ADVERSE EVENTS

The very uncontrolled nature of spontaneously reported data places great importance on the evaluation of submitted reports of adverse events. This process is perhaps most accurately characterized as a method, applied on a case-by-case basis, that is based on experience, knowledge of the medical product being monitored and awareness of the limitations of the data.

All reports from health professionals (direct reports) and specific reports from manufacturers are individually reviewed by an FDA health professional safety evaluator, with particular attention to all reported serious adverse events that are not in labeling in the case of pharmaceuticals[44]. All other reports are entered into the database for use in aggregate analysis. In focused evaluation of adverse events, the postmarketing surveillance database is searched for other reports, and further steps such as literature searches and use of medical product utilization databases may be taken.

Based on careful review of spontaneous reports, the FDA can initiate various actions, including a "Dear Health Professional" letter or Safety Alert; labeling, name or packaging change(s); conducting further epidemiologic investigations; requesting manufacturer-sponsored postmarketing studies; conducting inspections of manufacturers' facilities/records; or working with a manufacturer regarding possible withdrawal of a medical product from the market.

Four clinical synopses[44-55] provided by each of the four participating FDA Centers that outline examples of regulatory actions based on postmarketing surveillance are presented throughout the article. The clinical synopses demonstrate the step-wise process of spontaneous reports evaluation that is utilized at the FDA. In addition, these cases clearly illustrate that a single adverse event report from a health professional can often lead to an FDA action that has clinical importance.

At times signals generated by the spontaneous reporting system are of sufficient strength that further epidemiologic investigation is not necessary, a situation exemplified by the clinical synopses. However, non-epidemiologic types of studies may be indicated, such as those attempting to explain the etiology of eosinophilia-myalgia syndrome[50,53,54].

Should formal epidemiologic study be deemed useful in regard to an adverse event, well-validated methods can be utilized by FDA, industry, and academia in their investigations*. For example, FDA regulation of oral contraceptives has relied heavily on the findings of case-control and cohort studies[56].

*A future MEDWATCH Continuing Education Article will focus on the use of epidemiologic principles and methods in the study of medical product safety.

DISSEMINATION OF SAFETY-RELATED INFORMATION

Keeping medical product labeling/package inserts up to date is an ongoing, dynamic process that depends on new information gleaned from spontaneous adverse event reports. Remaining current with changes in medical product information can be an imposing task for the busy health professional. As a result, an important public health aspect of postmarketing surveillance is the dissemination of safety-related information to the clinical community.

The FDA, in concert with the product's manufacturer, informs health professionals of the most serious and pressing safety issues through such mechanisms as "Dear Health Professional" letters, Safety Alerts, Public Health Advisories, Talk Papers and Urgent Notices. Two recent examples demonstrating this educational process are outlined in TABLE 5.

TABLE 5

Examples of Safety-Related FDA Notifications

- **Retinal Photic Injuries From Operating Microscopes During Cataract Surgery:**

Despite all efforts taken to minimize the risks of retinal damage, retinal photic injuries from the light sources used in operating microscopes during cataract surgery and other intraocular procedures may occur. Several factors appear to be important determinants of photic retinal injury. These include: angle of light incidence, light intensity, exposure time, and intensity of the blue light component. FDA recommends several actions to reduce the risk of retinal photic injury and reminds physicians about the reporting requirements of the Safe Medical Devices Act of 1990. [October 16, 1995 FDA Public Health Advisory]

- **FDA Requires Labeling Change on Lindane-Containing Lice Treatments:**

Lindane is generally safe and effective when used according to the approved directions, but its overuse can be harmful. FDA has recommended labeling changes that encourage lindane's use only for patients who have either failed to respond to adequate doses of, or are intolerant of, other approved therapies. In addition, product labeling will advise health care providers and parents not to confuse prolonged itching with reinfestation. The label already warns parents that neurotoxicity is possible for certain patients, especially infants. [April 3, 1996 FDA Talk Paper]

The population of health professionals to whom individual notifications are distributed is not always universal, and is dependent on the medical product and the provider specialties most likely to be involved. As a result, other methods are used to reach the broadest possible health professional audience. The MEDWATCH column in the *FDA Medical Bulletin*, which is distributed to 1.2 million health professionals nationwide, seeks to enhance general awareness by summarizing the most recent notifications.

In addition, MEDWATCH utilizes its Partner program to disseminate new safety-related information. To date, over 100 health professional organizations have joined FDA as Partners and work with MEDWATCH to increase awareness of, and participation in, postmarketing surveillance. Notifications like Safety Alerts are provided to the Partners as they are released, with the information in turn distributed by the Partners to their members.

It is important for health professionals to be aware that not all changes in medical product information necessitate use of mechanisms such as a "Dear Health Professional" letter. These are reserved for only the most serious and pressing adverse events. While the *Physicians' Desk Reference*[R] contains official labeling for most drugs and can be reviewed periodically for changes, FDA is currently looking at other ways, including the Internet, by which new safety-related information can be made more readily available to health professionals.

SUMMARY

The effectiveness of a national postmarketing surveillance program is directly dependent on the active participation of health professionals. The limitations of premarketing clinical trials in detecting adverse events make the safety profile of any medical product an evolving, ongoing process contingent on the availability of up-to-date information derived from postmarketing clinical experience.

Despite the limitations of spontaneous reports, FDA's program for the surveillance of regulated medical product safety provides vital information of clinical importance. The identification of problems, and the subsequent dissemination of safety-related information to the clinical community at large, begins with reports from astute health professionals.

By viewing adverse event reporting as a professional responsibility, and recognizing that the quality of data generated from spontaneous reports is determined by the quality of the submitted information, health professionals can play a major role in improving the public health.

CLINICAL SYNOPSIS 4

DRUGS

Temafloxacin and Hemolytic Anemia

Temafloxacin, a fluoroquinolone antibiotic, was first marketed in January, 1992. By early April, FDA had received a few reports of hemolytic anemia occurring in patients treated with this drug. Over the next two months, many additional cases were reported, eventually totaling nearly 100. These provided a clear picture of what was subsequently called the "temafloxacin syndrome"[55].

The typical patient was a young woman with no underlying medical conditions who was treated for urinary tract infection with temafloxacin. Within 7-10 days of starting treatment, dark colored urine was often noted, sometimes with accompanying flank pain and chills. There was typically a drop in hemoglobin of 3 grams or greater. Acute renal failure developed in nearly two thirds, with hemodialysis usually required. Mild hepatobiliary changes were noted in half the patients, and coagulopathy in one third.

A subset of patients experienced the syndrome after their first dose of temafloxacin. That these patients were more likely to have had prior exposure to a fluoroquinolone antibiotic provided support for an antibody-mediated basis for massive hemolysis.

On the basis of spontaneously reported cases, the manufacturer, in consultation with FDA, voluntarily withdrew temafloxacin from the market worldwide in June, barely six months after initial marketing.

In 1994, FDA staff published a multicase review article describing the "temafloxacin syndrome"[55].

Acknowledgements

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Self-Assessment Questions

This program is sponsored by the Center for Drug Evaluation and Research (CDER), Food and Drug Administration.

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To receive certification of continuing medical education or pharmaceutical education credit the participant must:

- Answer at least 7 of the 10 self-assessment questions correctly
- Provide the required information on the answer sheet on the next page
- Participants receiving a failing grade will be notified

NOTE: THIS PROGRAM EXPIRES ON MARCH 31, 1998

1. Which of the following is NOT a known limitation of premarketing clinical trials?

A. Narrow population

B. Ability to detect common adverse events

C. Short duration

D. Small size

E. Narrow set of indications

2. Which of the following statements is FALSE?

A. Once a new medical product is marketed, the number of patients exposed to the product greatly increases

B. Premarketing clinical trials are conducted under controlled conditions in defined populations

C. The capability to detect adverse interactions with other medical products is generally enhanced once a new medical product is marketed

D. Once a new medical product is marketed, its initial labeling/ product information remains unchanged

E. Differences between the premarketing and postmarketing environments make adverse event detection and reporting by health professionals very important

3. Which of the following statements is FALSE with regard to MEDWATCH?

A. Causality is a prerequisite for reporting an adverse event to MEDWATCH

B. Any adverse event that is fatal, life-threatening or requires intervention to prevent permanent impairment or damage fulfills the MEDWATCH guideline for being considered serious

C. An increase in the reporting of serious adverse events is a MEDWATCH goal

D. The voluntary MEDWATCH form is to be used by health professionals in reporting adverse events related to all FDA-regulated medical products, except vaccines

E. Increasing understanding/ awareness of health professionals regarding medical product-induced disease is a MEDWATCH goal

4. Which of the following products does NOT require FDA safety and efficacy review prior to marketing:

A. Prescription drugs

B. Biologics

C. Dietary supplements

D. Over-the-counter (OTC) drugs

E. None of the above - they ALL require FDA safety and efficacy review prior to marketing

5. Which of the following represents a example of VOLUNTARY adverse event reporting?

A. User facility report of serious injury in a patient using a medical device

B. Quarterly periodic report from a manufacturer regarding a drug approved less than three years ago

C. Health professional report of a serious adverse event in a patient taking several different drugs

D. Manufacturer report of a serious and unexpected adverse event in a patient using a biologic

E. Health professional report of paralytic poliomyelitis occurring in a patient following vaccination against polio

6. All of the following are known limitations of spontaneous reports data EXCEPT:

A. Very costly to obtain

B. Lack of denominator data

C. Biases

D. Subjectivity of adverse event recognition

E. Underreporting

Continued on next page...

7. Which of the following statements is FALSE?

A. The importance of adverse event reports evaluation derives from the uncontrolled nature of spontaneously reported information

B. Literature searches and use of medical product utilization databases can be part of the adverse event reports evaluation process

C. Awareness of the limitations of spontaneous data is important in adverse event reports evaluation

D. Biological plausibility and strength of association are unimportant in adverse event reports evaluation

E. Full assessment of reported unlabeled serious adverse events is an important aspect of adverse event reports evaluation

8. All of the following are FDA actions that can result from careful analysis of spontaneous adverse event reports EXCEPT:

A. Conducting of further epidemiologic investigations

B. Requesting manufacturer-sponsored postmarketing studies

C. Changing labeling/product information

D. Working with the manufacturer on the issuance of a "Dear Health Professional" letter that outlines the serious safety issue involved

E. None of the above - ALL are actions the FDA can initiate in this regard

9. All of the following are known strengths of postmarketing surveillance systems based on spontaneous reports EXCEPT:

A. Hypothesis generation (signaling function)

B. Relatively immune to bias

C. Ongoing potential monitoring of all patients

D. Allow for major contributions by clinicians

E. Cost-effective in detecting rare, serious adverse events

10. All of the following are methods by which the FDA disseminates safety-related information to health professionals EXCEPT:

A. Work with manufacturers on the issuance of "Dear Health Professional" letters, Safety Alerts and Urgent Notices

B. Use of the MEDWATCH Partner program

C. Publications in the scientific literature

D. The MEDWATCH column in the *FDA Medical Bulletin*

E. None of the above - ALL are used by the FDA to inform health professionals of new safety information

Please Note:

- Do not mail answer sheet if it was previously faxed.
- Continuing education credit for this article can be awarded only once.
- To check on the status of your certificate, call Gale White at (301) 443-0117.

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ADVERSE EVENT REPORTING

MEDWATCH

APPLICATION FOR CONTINUING EDUCATION CREDIT

1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____ 7. _____ 8. _____ 9. _____ 10. _____

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The article met the stated learning objectives:

___ Strongly Agree ___ Agree ___ Disagree ___ Strongly Disagree ___ Cannot Decide

The information presented is relevant to my clinical practice: ___ Agree ___ Disagree

❑ Please send me a free copy of ***The FDA Desk Guide for Adverse Event and Product Problem Reporting*** (contains forms and instructions)

Mail the completed answer sheet by 3/31/98 to:

MEDWATCH, HF-2, Rm 9-57, FDA, 5600 Fishers Lane, Rockville, MD 20857 or FAX it to 1-800-FDA-0178.

A MEDWATCH CONTINUING EDUCATION ARTICLE

THE CLINICAL IMPACT OF ADVERSE EVENT REPORTING

The Food and Drug Administration (FDA)'s monitoring of the continued safety of marketed medical products depends greatly upon reporting of adverse events by health professionals. An understanding of how FDA uses this information, and of the limitations/strengths of the national postmarketing surveillance system, underscores the importance of this professional responsibility to the public health.

DEPARTMENT OF HEALTH & HUMAN SERVICES

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Complimentary CE Article

THE CLINICAL IMPACT OF ADVERSE EVENT REPORTING

FDA

Exhibit D

Guidance for Industry

E2E Pharmacovigilance Planning

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2005
ICH

Guidance for Industry

E2E Pharmacovigilance Planning

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April 2005
ICH

Contains Nonbinding Recommendations

TABLE OF CONTENTS

Contains Nonbinding Recommendations

Guidance for Industry[1]

E2E Pharmacovigilance Planning

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION (1, 1.1) [2]

This guidance is intended to aid in planning pharmacovigilance activities, especially in preparation for the early postmarketing period of a new drug (in this guidance, the term *drug* denotes chemical entities, biotechnology-derived products, and vaccines). The main focus of this guidance is on a safety specification and pharmacovigilance plan that might be submitted at the time of license application. The guidance can be used by sponsors to develop a stand-alone document for regions that prefer this approach or to provide guidance on incorporation of elements of the safety specification and pharmacovigilance plan into the Common Technical Document (CTD).

The guidance describes a method for summarizing the important identified risks of a drug, important potential risks, and important missing information, including the potentially at-risk populations and situations where the product is likely to be used that have not been studied preapproval. It proposes a structure for a pharmacovigilance plan and sets out principles of good practice for the design and conduct of observational studies. It does not describe other methods to reduce risks from drugs, such as risk communication. The guidance takes into consideration ongoing work in the three regions and beyond on these issues.

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[1] This guidance was developed within the Expert Working Group (Efficacy) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and has been subject to consultation by the regulatory parties, in accordance with the ICH process. This document has been endorsed by the ICH Steering Committee at *Step 4* of the ICH process, November 2004. At *Step 4* of the process, the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan, and the United States.

[2] Arabic numbers reflect the organizational breakdown in the document endorsed by the ICH Steering Committee at Step 4 of the ICH process, November 2004.

This guidance does not cover the entire scope of pharmacovigilance. It uses the World Health Organization (WHO) definition of the term *pharmacovigilance* as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems." This definition encompasses the use of pharmacoepidemiological studies.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

A. Background (1.2)

The decision to approve a drug is based on its having a satisfactory balance of benefits and risks within the conditions specified in the product labeling. This decision is based on the information available at the time of approval. The knowledge related to the safety profile of the product can change over time through expanded use in terms of patient characteristics and the number of patients exposed. In particular, during the early postmarketing period, the product might be used in settings different from clinical trials and a much larger population might be exposed in a relatively short timeframe.

Once a product is marketed, new information will be generated, which can have an impact on the benefits or risks of the product; evaluation of this information should be a continuing process, in consultation with regulatory authorities. Detailed evaluation of the information generated through pharmacovigilance activities is important for all products to ensure their safe use. The benefit-risk balance can be improved by reducing risks to patients through effective pharmacovigilance that can enable information feedback to the users of medicines in a timely manner.

Industry and regulators have identified the need for better and earlier planning of pharmacovigilance activities before a product is approved or a license is granted. This ICH guidance has been developed to encourage harmonization and consistency and prevent duplication of effort and could be of benefit to public health programs throughout the world as they consider new drugs in their countries.

B. Scope of the Guidance (1.3)

The guidance could be most useful for new chemical entities, biotechnology-derived products, and vaccines, as well as for significant changes in established products (e.g., new dosage form, new route of administration, or new manufacturing process for a biotechnology-derived product) and for established products that are to be introduced to new populations or in significant new indications or where a new major safety concern has arisen.

Contains Nonbinding Recommendations

The purpose of this guidance is to propose a structure for a pharmacovigilance plan and a safety specification that summarizes the identified and potential risks of the product to be addressed in the plan. The guidance is divided into the following sections:

- Safety specification
- Pharmacovigilance plan
- Annex — Pharmacovigilance Methods

It is recommended that company pharmacovigilance experts get involved early in product development. Planning and dialogue with regulators should also start long before license application. A safety specification and pharmacovigilance plan can also be developed for products already on the market (e.g., new indication or major new safety concern). The plan could be used as the basis for discussion of pharmacovigilance activities with regulators in the different ICH regions and beyond.

For products with important identified risks, important potential risks or important missing information, the pharmacovigilance plan should include additional actions designed to address these concerns. For products for which no special concerns have arisen, routine pharmacovigilance as described in section III.A.2 (3.1.2) of this guidance should be sufficient for postapproval safety monitoring, without the need for additional actions (e.g., safety studies).

During the course of implementing the various components of the plan, any important emerging benefit or risk information should be discussed and used to revise the plan.

The following principles underpin this guidance:

- Planning of pharmacovigilance activities throughout the product life-cycle
- Science-based approach to risk documentation
- Effective collaboration between regulators and industry
- Applicability of the pharmacovigilance plan across the three ICH regions

II. SAFETY SPECIFICATION (2)

The safety specification should be a summary of the important identified risks of a drug, important potential risks, and important missing information. It should also address the populations potentially at-risk (where the product is likely to be used), and outstanding safety questions that warrant further investigation to refine understanding of the benefit-risk profile during the postapproval period. This safety specification is intended to help industry and regulators identify any need for specific data collection and also to facilitate the construction of the pharmacovigilance plan. The safety specification can be built initially during the premarketing phase and, at the time approval is sought, it should reflect the status of issues that were being followed during development.

The Common Technical Document (CTD), especially the Overview of Safety (2.5.5), Benefits and Risks Conclusions (2.5.6), and the Summary of Clinical Safety (2.7.4) sections, includes information relating to the safety of the product and should be the basis of the safety issues identified in the safety specification. Sponsors should support the safety specification with

references to specific pages of the CTD or other relevant documents. The safety specification can be a stand-alone document, usually in conjunction with the pharmacovigilance plan, but elements can also be incorporated into the CTD. The length of the document will generally depend on the product and its development program. Appendices can be added if it is considered important to provide a more detailed explanation of important risks or analyses.

A. Elements of the Safety Specification (2.1)

It is recommended that sponsors follow the structure of elements provided below when compiling the safety specification. The elements of the safety specification that are included are only a guide. The safety specification can include additional elements, depending on the nature of the product and its development program. Conversely, for products already on the market with emerging new safety concerns, only a subset of the elements might be relevant.

The focus of the safety specification should be on the identified risks, important potential risks, and important missing information. The following elements should be considered for inclusion.

1. Nonclinical (2.1.1)

Within the Specification, this section should present nonclinical safety findings that have not been adequately addressed by clinical data, for example:

- Toxicity (including repeat-dose toxicity, reproductive/developmental toxicity, nephrotoxicity, hepatotoxicity, genotoxicity, carcinogenicity, etc.)
- General pharmacology (cardiovascular, including QT interval prolongation; nervous system; etc.)
- Drug interactions
- Other toxicity-related information or data

If the product is intended for use in special populations, consideration should be given to whether specific nonclinical data needs exist.

2. Clinical (2.1.2)

a. Limitations of the human safety database

Limitations of the safety database (e.g., related to the size of the study population, study inclusion/exclusion criteria) should be considered, and the implications of such limitations with respect to predicting the safety of the product in the marketplace should be explicitly discussed. Particular reference should be made to populations likely to be exposed during the intended or expected use of the product in medical practice.

The worldwide experience should be briefly discussed, including:

- The extent of the worldwide exposure
- Any new or different safety issues identified
- Any regulatory actions related to safety

b. Populations not studied in the preapproval phase

The specification should discuss which populations have not been studied or have only been studied to a limited degree in the preapproval phase. The implications of this with respect to predicting the safety of the product in the marketplace should be explicitly discussed (CTD 2.5.5). Populations to be considered should include (but might not be limited to):

- Children
- The elderly
- Pregnant or lactating women
- Patients with relevant co-morbidity such as hepatic or renal disorders
- Patients with disease severity different from that studied in clinical trials
- Sub-populations carrying known and relevant genetic polymorphism
- Patients of different racial and/or ethnic origins

c. Adverse events (AEs)/adverse drug reactions (ADRs)

This section should list the important identified and potential risks that require further characterization or evaluation. Specific references should be made to guide a reviewer to where clinical safety data are presented (e.g., relevant sections of the CTD 2.5.5 and 2.7.4). Discussion of risk factors and potential mechanisms that apply to identified AEs/ADRs should draw on information from any part of the CTD (nonclinical and clinical) and other relevant information, such as other drug labels, scientific literature, and postmarketing experience.

Identified risks for further evaluation

More detailed information should be included on the most important identified AEs/ADRs, which would include those that are serious or frequent and that also might have an impact on the balance of benefits and risks of the product. This information should include evidence bearing on a causal relationship, severity, seriousness, frequency, reversibility and at-risk groups, if available. Risk factors and potential mechanisms should be discussed. These AEs/ADRs should usually call for further evaluation as part of the pharmacovigilance plan (e.g., frequency in normal conditions of use, severity, outcome, at-risk groups).

Potential risks for further evaluation

Important potential risks should be described in this section. The evidence that led to the conclusion that there was a potential risk should be presented. It is anticipated that for any important potential risk, there should be further evaluation to characterize the association.

d. Identified and potential interactions, including food-drug and drug-drug interactions

Identified and potential pharmacokinetic and pharmacodynamic interactions should be discussed. For each, the evidence supporting the interaction and possible mechanism should be summarized, and the potential health risks posed for the different indications and in the different populations should be discussed.

e. Epidemiology

The epidemiology of the indication(s) should be discussed. This discussion should include incidence, prevalence, mortality and relevant co-morbidity, and should take into account whenever possible stratification by age, sex, and racial and/or ethnic origin. Differences in the epidemiology in the different regions should be discussed (because the epidemiology of the indication(s) may vary across regions), if this information is available.

In addition, for important adverse events that may require further investigation, it is useful to review the incidence rates of these events among patients in whom the drug is indicated (i.e., the background incidence rates). For example, if condition X is an important adverse event in patients who are treated with drug Y for disease Z, then it is useful to review the incidence of condition X in patients with disease Z who are not treated with drug Y; this is the background rate of condition X among patients with disease Z. Information on risk factors for an adverse event (condition X) would also be useful to include, if available.

f. Pharmacological class effects

The safety specification should identify risks believed to be common to the pharmacological class.

B. Summary (2.2)

At the end of the safety specification, a summary should be provided of the:

- Important identified risks
- Important potential risks
- Important missing information

Sponsors are encouraged to summarize specific ongoing safety issues on an issue-by-issue basis, including both nonclinical and clinical data that are pertinent to the problem.

III. PHARMACOVIGILANCE PLAN (3)

This section gives guidance on the structure of a pharmacovigilance plan. The pharmacovigilance plan should be based on the safety specification. The specification and plan can be written as two parts of the same document. The plan would normally be developed by the sponsor and can be discussed with regulators during product development, prior to approval (i.e., when the marketing application is submitted) of a new product, or when a safety concern arises postmarketing. It can be a stand-alone document, but elements could also be incorporated into the CTD.

For products for which no special concerns have arisen, routine pharmacovigilance as described in section III.A.2 (3.1.2) of this guidance should be sufficient for postapproval safety monitoring, without the need for additional actions (e.g., safety studies). However, for products with

important identified risks, important potential risks, or important missing information, additional actions designed to address these concerns should be considered.

The length of the document will likely depend on the product and its development program. The pharmacovigilance plan should be updated as important information on safety becomes available and milestones are reached.

A. Structure of the Pharmacovigilance Plan (3.1)

Outlined below is a suggested structure for the pharmacovigilance plan. The structure can be varied depending on the product in question and the issues identified in the safety specification.

1. Summary of Ongoing Safety Issues (3.1.1)

At the beginning of the pharmacovigilance plan, a summary should be provided of the:

- Important identified risks
- Important potential risks
- Important missing information

This is important if the pharmacovigilance plan is a separate document from the safety specification.

2. Routine Pharmacovigilance Practices (3.1.2)

Routine pharmacovigilance should be conducted for all medicinal products, regardless of whether or not additional actions are appropriate as part of a pharmacovigilance plan. This routine pharmacovigilance should include the following:

- Systems and processes that ensure that information about all suspected adverse reactions that are reported to the personnel of the company are collected and collated in an accessible manner

- The preparation of reports for regulatory authorities:
  - — Expedited adverse drug reaction (ADR) reports
  - — Periodic safety update reports (PSURs)

- Continuous monitoring of the safety profile of approved products including signal detection, issue evaluation, updating of labeling, and liaison with regulatory authorities

- Other requirements, as defined by local regulations

In some ICH regions, there might be a regulatory requirement to present within the pharmacovigilance plan an overview of the company's organization and practices for conducting pharmacovigilance. In the absence of such a requirement, a statement that the company's routine

pharmacovigilance practices include the elements outlined in the bulleted list above should be sufficient.

3. Action Plan for Safety Issues (3.1.3)

The plan for each important safety issue should be presented and justified according to the following structure:

- Safety issue
- Objective of proposed action(s)
- Action(s) proposed
- Rationale for proposed action(s)
- Monitoring by the sponsor for safety issue and proposed action(s)
- Milestones for evaluation and reporting

Any protocols for specific studies can be provided in the CTD section 5.3.5.4 Other Clinical Study Reports or other sections as appropriate (e.g., Module 4 if the study is a nonclinical study).

4. Summary of Actions To Be Completed, Including Milestones (3.1.4)

An overall pharmacovigilance plan for the product bringing together the actions for all individual safety issues should be presented. Whereas section 3.1.3 suggests presenting an action plan by ongoing safety issue, for this section the pharmacovigilance plan for the product should be organized in terms of the actions to be undertaken and their milestones. The reason for this is that one proposed action (e.g., a prospective safety cohort study) could address more than one of the identified issues.

It is recommended that milestones for completion of studies and other evaluations, and for submission of safety results, be included in the pharmacovigilance plan. In developing these milestones, one should consider when:

- Exposure to the product will have reached a level sufficient to allow potential identification/characterization of the AEs/ADRs of concern or resolution of a particular concern, and/or
- The results of ongoing or proposed safety studies are expected to be available.

These milestones might be aligned with regulatory milestones (e.g., PSURs, annual reassessment and license renewals) and used to revise the pharmacovigilance plan.

B. Pharmacovigilance Methods (3.2)

The best method to address a specific situation can vary, depending on the product, the indication, the population being treated and the issue to be addressed. The method chosen can also depend on whether an identified risk, potential risk, or missing information is the issue and whether signal detection, evaluation, or safety demonstration is the main objective of further study. When choosing a method to address a safety concern, sponsors should employ the most

appropriate design. The Annex provides a summary of the key methods used in pharmacovigilance. This is provided to aid sponsors considering possible methods to address specific issues identified by the safety specification. This list is not all-inclusive, and sponsors should use the most up-to-date methods that are relevant and applicable.

Design and Conduct of Observational Studies (3.2.1)

Carefully designed and conducted pharmacoepidemiological studies, specifically observational (noninterventional, nonexperimental) studies, are important tools in pharmacovigilance. In observational studies, the investigator "observes and evaluates results of ongoing medical care without 'controlling' the therapy beyond normal medical practice."[1]

Before the observational study that is part of a pharmacovigilance plan commences, a protocol should be finalized. Experts from relevant disciplines (e.g., pharmacovigilance experts, pharmacoepidemiologists and biostatisticians) should be consulted. It is recommended that the protocol be discussed with the regulatory authorities before the study starts. It is also suggested that the circumstances in which a study should be terminated early be discussed with regulatory authorities and documented in advance. A study report after completion, and interim reports if appropriate, should be submi tted to the authorities according to the milestones within the pharmacovigilance plan.

Study protocols should, as a minimum, include the study aims and objectives, the methods to be used, and the plan for analysis. The final study report should accurately and completely present the study objectives, methods, results, and the principal investigator's interpretation of the findings.

It is recommended that the sponsor follow good epidemiological practice for observational studies and also internationally accepted guidelines, such as the guidelines endorsed by the International Society for Pharmacoepidemiology.[2] In some of the ICH regions, local laws and guidelines also apply to the design and conduct of observational studies and should be followed.

The highest possible standards of professional conduct and confidentiality should always be maintained, and any relevant national legislation on data protection followed.

IV. REFERENCES (4)

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Contains Nonbinding Recommendations

ANNEX — PHARMACOVIGILANCE METHODS

1. Passive Surveillance

- **Spontaneous Reports**

A spontaneous report is an unsolicited communication by healthcare professionals or consumers to a company, regulatory authority or other organization (e.g., WHO, regional centers, poison control center) that describes one or more adverse drug reactions in a patient who was given one or more medicinal products and that does not derive from a study or any organized data collection scheme.[1]

Spontaneous reports play a major role in the identification of safety signals once a drug is marketed. In many instances, a company can be alerted to rare adverse events that were not detected in earlier clinical trials or other premarketing studies. Spontaneous reports can also provide important information on at-risk groups, risk factors, and clinical features of known serious adverse drug reactions. Caution should be exercised in evaluating spontaneous reports, especially when comparing drugs. The data accompanying spontaneous reports are often incomplete, and the rate at which cases are reported is dependent on many factors including the time since launch, pharmacovigilance-related regulatory activity, media attention, and the indication for use of the drug.[2, 3, 4, 5]

Systematic Methods for the Evaluation of Spontaneous Reports

More recently, systematic methods for the detection of safety signals from spontaneous reports have been used. Many of these techniques are still in development and their usefulness for identifying safety signals is being evaluated. These methods include the calculation of the proportional reporting ratio, as well as the use of Bayesian and other techniques for signal detection.[6, 7, 8] Data mining techniques have also been used to examine drug-drug interactions.[9] Data mining techniques should always be used in conjunction with, and not in place of, analyses of single case reports. Data mining techniques facilitate the evaluation of spontaneous reports by using statistical methods to detect potential signals for further evaluation. This tool does not quantify the magnitude of risk, and caution should be exercised when comparing drugs. Further, when using data mining techniques, consideration should be given to the threshold established for detecting signals, since this will have implications for the sensitivity and specificity of the method (a high threshold is associated with high specificity and low sensitivity). Confounding factors that influence spontaneous adverse event reporting are not removed by data mining. Results of data mining should be interpreted with the knowledge of the weaknesses of the spontaneous reporting system and, more specifically, the large differences in the ADR reporting rate among different drugs and the many potential biases inherent in spontaneous reporting. All signals should be evaluated recognizing the possibility of false positives. In addition, the absence of a signal does not mean that a problem does not exist.

- **Case Series**

Series of case reports can provide evidence of an association between a drug and an adverse event, but they are generally more useful for generating hypotheses than for verifying an association between drug exposure and outcome. There are certain distinct adverse events known to be associated more frequently with drug therapy, such as anaphylaxis, aplastic anemia, toxic epidermal necrolysis and Stevens-Johnson Syndrome.[10, 11] Therefore, when events such as these are spontaneously reported, sponsors should place more emphasis on these reports for detailed and rapid follow-up.

2. Stimulated Reporting

Several methods have been used to encourage and facilitate reporting by health professionals in specific situations (e.g., in-hospital settings) for new products or for limited time periods.[12] Such methods include on-line reporting of adverse events and systematic stimulation of reporting of adverse events based on a predesigned method. Although these methods have been shown to improve reporting, they are not devoid of the limitations of passive surveillance, especially selective reporting and incomplete information.

During the early postmarketing phase, companies might actively provide health professionals with safety information, and at the same time encourage cautious use of new products and the submission of spontaneous reports when an adverse event is identified. A plan can be developed before the product is launched (e.g., through site visits by company representatives, by direct mailings or faxes, etc.). Stimulated adverse event reporting in the early postmarketing phase can lead companies to notify healthcare professionals of new therapies and provide safety information early in use by the general population (e.g., Early Post-marketing Phase Vigilance, EPPV in Japan). This should be regarded as a form of spontaneous event reporting; thus, data obtained from stimulated reporting cannot be used to generate accurate incidence rates, but reporting rates can be estimated.

3. Active Surveillance

Active surveillance, in contrast to passive surveillance, seeks to ascertain completely the number of adverse events via a continuous preorganized process. An example of active surveillance is the follow-up of patients treated with a particular drug through a risk management program. Patients who fill a prescription for this drug may be asked to complete a brief survey form and give permission for later contact.[13] In general, it is more feasible to get comprehensive data on individual adverse event reports through an active surveillance system than through a passive reporting system.

- **Sentinel Sites**

Active surveillance can be achieved by reviewing medical records or interviewing patients and/or physicians in a sample of sentinel sites to ensure complete and accurate data on reported adverse events from these sites. The selected sites can provide information, such as data from specific patient subgroups, that would not be available in a passive spontaneous reporting

system. Further, information on the use of a drug, such as abuse, can be targeted at selected sentinel sites[14]. Some of the major weaknesses of sentinel sites are problems with selection bias, small numbers of patients, and increased costs. Active surveillance with sentinel sites is most efficient for those drugs used mainly in institutional settings such as hospitals, nursing homes, hemodialysis centers, etc. Institutional settings can have a greater frequency of use for certain drug products and can provide an infrastructure for dedicated reporting. In addition, automatic detection of abnormal laboratory values from computerized laboratory reports in certain clinical settings can provide an efficient active surveillance system. Intensive monitoring of sentinel sites can also be helpful in identifying risks among patients taking orphan drugs.

- **Drug Event Monitoring**

Drug event monitoring is a method of active pharmacovigilance surveillance. In drug event monitoring, patients might be identified from electronic prescription data or automated health insurance claims. A follow-up questionnaire can then be sent to each prescribing physician or patient at prespecified intervals to obtain outcome information. Information on patient demographics, indication for treatment, duration of therapy (including start dates), dosage, clinical events, and reasons for discontinuation can be included in the questionnaire.[12, 15, 16, 17] Limitations of drug event monitoring can include poor physician and patient response rates and the unfocused nature of data collection, which can obscure important signals. In addition, maintenance of patient confidentiality might be a concern. On the other hand, more detailed information on adverse events from a large number of physicians and/or patients might be collected.

- **Registries**

A registry is a list of patients presenting with the same characteristic(s). This characteristic can be a disease (disease registry) or a specific exposure (drug registry). Both types of registries, which only differ by the type of patient data of interest, can collect a battery of information using standardized questionnaires in a prospective fashion. Disease registries, such as registries for blood dyscrasias, severe cutaneous reactions, or congenital malformations can help collect data on drug exposure and other factors associated with a clinical condition. A disease registry might also be used as a base for a case-control study comparing the drug exposure of cases identified from the registry and controls selected from either patients with another condition within the registry, or patients outside the registry.

Exposure (drug) registries address populations exposed to drugs of interest (e.g., registry of rheumatoid arthritis patients exposed to biological therapies) to determine if a drug has a special impact on this group of patients. Some exposure (drug) registries address drug exposures in specific populations, such as pregnant women. Patients can be followed over time and included in a cohort study to collect data on adverse events using standardized questionnaires. Single cohort studies can measure incidence, but, without a comparison group, cannot provide proof of association. However, they can be useful for signal amplification, particularly for rare outcomes. This type of registry can be very valuable when examining the safety of an orphan drug indicated for a specific condition.

4. Comparative Observational Studies

Traditional epidemiologic methods are a key component in the evaluation of adverse events. There are a number of observational study designs that are useful in validating signals from spontaneous reports or case series. Major types of these designs are cross-sectional studies, case-control studies, and cohort studies (both retrospective and prospective).[12, 15]

- **Cross-sectional Study (Survey)**

Data collected on a population of patients at a single point in time (or interval of time) regardless of exposure or disease status constitute a cross-sectional study. These types of studies are primarily used to gather data for surveys or for ecological analyses. The major drawback of cross-sectional studies is that the temporal relationship between exposure and outcome cannot be directly addressed. These studies are best used to examine the prevalence of a disease at one time point or to examine trends over time, when data for serial time points can be captured. These studies can also be used to examine the crude association between exposure and outcome in ecologic analyses. Cross-sectional studies are best utilized when exposures do not change over time.

- **Case-control Study**

In a case-control study, cases of disease (or events) are identified. Controls, or patients without the disease or event of interest, are then selected from the source population that gave rise to the cases. The controls should be selected in such a way that the prevalence of exposure among the controls represents the prevalence of exposure in the source population. The exposure status of the two groups is then compared using the odds ratio, which is an estimate of the relative risk of disease in the two groups. Patients can be identified from an existing database or using data collected specifically for the purpose of the study of interest. If safety information is sought for special populations, the cases and controls can be stratified according to the population of interest (the elderly, children, pregnant women, etc.). For rare adverse events, existing large population-based databases are a useful and efficient means of providing needed drug exposure and medical outcome data in a relatively short period of time. Case-control studies are particularly useful when the goal is to investigate whether there is an association between a drug (or drugs) and one specific rare adverse event, as well as to identify risk factors for adverse events. Risk factors can include conditions such as renal and hepatic dysfunction, that might modify the relationship between the drug exposure and the adverse event. Under specific conditions, a case-control study can provide the absolute incidence rate of the event. If all cases of interest (or a well-defined fraction of cases) in the catchment area are captured and the fraction of controls from the source population is known, an incidence rate can be calculated.

- **Cohort Study**

In a cohort study, a population-at-risk for the disease (or event) is followed over time for the occurrence of the disease (or event). Information on exposure status is known throughout the follow-up period for each patient. A patient might be exposed to a drug at one time during follow-up, but nonexposed at another time point. Since the population exposure during follow-up

is known, incidence rates can be calculated. In many cohort studies involving drug exposure, comparison cohorts of interest are selected on the basis of drug use and followed over time. Cohort studies are useful when there is a need to know the incidence rates of adverse events in addition to the relative risks of adverse events. Multiple adverse events can also be investigated using the same data source in a cohort study. However, it can be difficult to recruit sufficient numbers of patients who are exposed to a drug of interest (such as an orphan drug) or to study very rare outcomes. Like case-control studies, the identification of patients for cohort studies can come from large automated databases or from data collected specifically for the study at hand. In addition, cohort studies can be used to examine safety issues in special populations (the elderly, children, patients with co-morbid conditions, pregnant women) through over-sampling of these patients or by stratifying the cohort if sufficient numbers of patients exist.

There are several automated databases available for pharmacoepidemiologic studies.[12, 15, 18] They include databases that contain automated medical records or automated accounting/billing systems. Databases that are created from accounting/billing systems might be linked to pharmacy claims and medical claims databases. These datasets might include millions of patients. Since they are created for administrative or billing purposes, they might not have the detailed and accurate information needed for some research, such as validated diagnostic information or laboratory data. Although medical records can be used to ascertain and validate test results and medical diagnoses, one should be cognizant of the privacy and confidentiality regulations that apply to patient medical records.

5. Targeted Clinical Investigations

When significant risks are identified from preapproval clinical trials, further clinical studies might be called for to evaluate the mechanism of action for the adverse reaction. In some instances, pharmacodynamic and pharmacokinetic studies might be conducted to determine whether a particular dosing instruction can put patients at an increased risk of adverse events. Genetic testing can also provide clues about which group of patients might be at an increased risk of adverse reactions. Furthermore, based on the pharmacological properties and the expected use of the drug in general practice, conducting specific studies to investigate potential drug-drug interactions and food-drug interactions might be called for. These studies can include population pharmacokinetic studies and drug concentration monitoring in patients and normal volunteers.

Sometimes, potential risks or unforeseen benefits in special populations might be identified from preapproval clinical trials, but cannot be fully quantified due to small sample sizes or the exclusion of subpopulations of patients from these clinical studies. These populations might include the elderly, children, or patients with renal or hepatic disorder. Children, the elderly, and patients with co-morbid conditions might metabolize drugs differently than patients typically enrolled in clinical trials. Further clinical trials might be used to determine and to quantify the magnitude of the risk (or benefit) in such populations.

To elucidate the benefit-risk profile of a drug outside of the formal/traditional clinical trial setting and/or to fully quantify the risk of a critical but relatively rare adverse event, a large simplified trial might be conducted. Patients enrolled in a large simplified trial are usually randomized to avoid selection bias. In this type of trial, though, the event of interest will be

focused to ensure a convenient and practical study. One limitation of this method is that the outcome measure might be too simplified and this might have an impact on the quality and ultimate usefulness of the trial. Large, simplified trials are also resource-intensive.

6. Descriptive Studies

Descriptive studies are an important component of pharmacovigilance, although not for the detection or verification of adverse events associated with drug exposures. These studies are primarily used to obtain the background rate of outcome events and/or establish the prevalence of the use of drugs in specified populations.

- **Natural History of Disease**

The science of epidemiology originally focused on the natural history of disease, including the characteristics of diseased patients and the distribution of disease in selected populations, as well as estimating the incidence and prevalence of potential outcomes of interest. These outcomes of interest now include a description of disease treatment patterns and adverse events. Studies that examine specific aspects of adverse events, such as the background incidence rate of or risk factors for the adverse event of interest, can be used to assist in putting spontaneous reports into perspective.[15] For example, an epidemiologic study can be conducted using a disease registry to understand the frequency at which the event of interest might occur in specific subgroups, such as patients with concomitant illnesses.

- **Drug Utilization Study**

Drug utilization studies (DUS) describe how a drug is marketed, prescribed, and used in a population, and how these factors influence outcomes, including clinical, social, and economic outcomes.[12] These studies provide data on specific populations, such as the elderly, children, or patients with hepatic or renal dysfunction, often stratified by age, gender, concomitant medication, and other characteristics. DUS can be used to determine if a product is being used in these populations. From these studies denominator data can be developed for use in determining rates of adverse drug reactions. DUS have been used to describe the effect of regulatory actions and media attention on the use of drugs, as well as to develop estimates of the economic burden of the cost of drugs. DUS can be used to examine the relationship between recommended and actual clinical practice. These studies can help to determine whether a drug has the potential for drug abuse by examining whether patients are taking escalating dose regimens or whether there is evidence of inappropriate repeat prescribing. Important limitations of these studies can include a lack of clinical outcome data or information of the indication for use of a product.

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Exhibit E

UNITED STATES DISTRICT COURT

DISTRICT OF NEW JERSEY

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IN RE: BENICAR (OLMESARTAN) PRODUCTS LIABILITY LITIGATION	*	CIVIL NO. 15-2606(RBK)(JS)
	*	JUDGE KUGLER
THIS DOCUMENT RELATES TO ALL CASES	*	MAG. JUDGE SCHNEIDER

* * * * * * * * * * * * * * * * * * * *

* PROTECTED INFORMATION *

DEPOSITION OF DANIEL A. LEFFLER, M.D.

ROBINS & KAPLAN

800 Boylston Street

Boston, Massachusetts

February 3, 2017 8:32 a.m.

Maryellen Coughlin, RPR/CRR

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describing the clinical features of sprue-like enteropathy associated with olmesartan?

A. Yes.

Q. And do you agree that these are the clinical features of sprue-like enteropathy?

MS. SUTTON: Objection, form, foundation.

A. So I think that these -- that many patients in many cases that I've seen with olmesartan enteropathy have these features, some or all of them.

I don't think this is a completely exhaustive list of all the features of olmesartan enteropathy, and I don't think that you need all these features to be present to have olmesartan enteropathy, but I think this is a representative table.

Q. And have you published a representative table of characteristics of sprue-like enteropathy with olmesartan?

A. I have not.

Q. But you have -- you have added additional clinical features that you consider to be associated with sprue-like enteropathy?

MS. SUTTON: Objection, form.

A. Based on subsequent reports in the literature and my own clinical experience, yes, I think that there are -- that it is acknowledged that there's a wider spectrum of presentation than was initially noted in this first 2012 article.

Q. And what features would you add to Exhibit No. 3 --

MS. SUTTON: Objection, form.

Q. -- that is not included by the authors of Exhibit No. 2?

MS. SUTTON: Objection, form. You can answer.

A. So I think that there are -- I think the way this table is, but it's not entirely clear what symptoms you need or what tests you need or don't need to diagnose olmesartan enteropathy.

I think gastrointestinal symptoms, as is sort of noted by the e.g., they don't suggest that the chronic diarrhea, weight loss and steatorrhea are the only symptoms you can have. The other ones that seem to be common are vomiting and abdominal pain.

At this point, you don't need a

Q. And you recognize that the ROADMAP study is a double-blind, randomized controlled trial, correct?

A. That is correct.

Q. And in the hierarchy of evidence, a randomized controlled trial is the highest level of evidence, correct?

A. So randomized controlled trials are an excellent study design, but they are only as good looking as looking at -- as they're powered for the outcome you're addressing. So they're excellent at looking at -- if they're designed properly, they're excellent for interpreting the primary outcome of the study.

For secondary outcomes and adverse events, they are often insufficient. And this is why we do things like MedWatch reports, 'cause in even the largest clinical trial, randomized clinical trial, pivotal clinical trial, uncommon and unexpected adverse events are often not seen.

Q. Dr. Leffler, you understand what evidence-based medicine is, don't you?

A. I do.

Q. And you agree that a fundamental principle of evidence-based medicine is the

hierarchy of evidence?

MS. SUTTON: Objection, form, asked and answered.

A. I do.

(Whereupon, Deposition Exhibit 35, "Hierarchy of Scientific Evidence", was marked for identification.)

BY MR. CHRISTIAN

Q. I hand you what's been marked as Exhibit No. 35. You've seen representations of the hierarchy of scientific evidence like this before, Doctor, have you not?

A. I have.

Q. And this shows that the strongest in the top of the hierarchy of scientific evidence is meta-analyses and systematic reviews, correct?

A. That is correct.

Q. And the next level down is randomized controlled trials, correct?

A. Correct.

Q. And the very bottom, weakest category, are case reports, opinion papers and letters, correct?

A. That's correct.

(Whereupon, Deposition Exhibit 41, Index entitled "Benicar, Controlled Epidemiologic Studies of OLM use and Risk of SE/Chronic serious diarrhea", was marked for identification.)

BY MR. CHRISTIAN

Q. I've marked as Exhibit No. 41 the five controlled epidemiologic studies of olmesartan use and risk of sprue-like enteropathy that we've discussed, ROADMAP, Greywoode, Padwal, Lagana and Basson, and out of those five controlled epidemiologic studies, only one of the five shows a statistically significant association between olmesartan and sprue-like enteropathy, correct?

MS. SUTTON: Just a second. Objection, form, foundation. Objection to the attorney created document in Exhibit 41.

A. So the Basson study was the only one of these studies with significant enough power and duration to detect a difference. In the other studies, many of them show a trend, although it does not reach statistical significance, and that is exactly what you would expect to see with outcomes that are -- with

outcomes when you look at studies that aren't powered to detect them.

Q. So the only study that you can tell us today that is a controlled epidemiologic study that has a statistically significant association between olmesartan use and sprue-like enteropathy is the Basson study; is that correct?

MS. SUTTON: Objection, form, foundation.

A. That is correct.

Q. Now, you also looked at some -- you published some -- or, sorry, you reference some published case reports in your report, correct?

A. That is correct.

Q. Did you review -- did you actually analyze every single one of those case reports that you cited, like actually read the entire report?

A. Everything in my -- everything that I reference and cited in my review I did read.

Q. And many of them are in foreign languages. Did you have those translated?

A. Where necessary, I did. Many of them also exist online in a English version.

Q. Okay. So some of them you did have

Exhibit F

Olmesartan and Intestinal Adverse Effects in the ROADMAP Study

To the Editor: We read the article by Rubio-Tapia and colleagues[1] with great interest. In this article, the authors describe the occurrence of severe spruelike enteropathy in 22 patients, all of whom received olmesartan (predominantly 40 mg/d) besides other drugs. All patients had long-lasting diarrhea (3-53 months) and weight loss (2.5-50 kg). Many patients also experienced nausea and vomiting (68% of patients), abdominal pain (50%), bloating (41%), and fatigue (68%). Interestingly, these symptoms disappeared after use of olmesartan was stopped. The authors draw the conclusion that olmesartan may directly be involved in spruelike enteropathy. However, our observation in a large group of diabetic patients treated with 40 mg of olmesartan daily does not support this conclusion. We detected no association between treatment with 40 mg of olmesartan once daily and the occurrence of intestinal adverse effects in 2232 patients treated for a median of 3.2 years in the Randomised Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study.

The largest prospective, randomized, double-blind study with olmesartan is the ROADMAP study.[2,3] In this study, patients with type 2 diabetes were treated with 40 mg of olmesartan (n=2232) or placebo (n=2215) once daily for a median of 3.2 years, and the occurrence of microalbuminuria (interpreted as an early sign of kidney and vascular damage) was the primary end point. We now analyzed the treatment-emergent adverse events (TEAEs) reported by the study physicians. For this analysis, we selected all intestinal illnesses that typically present with diarrhea and selected all symptoms and conditions that were related to abdominal discomfort, such as pain (Table). A total of 78 patients (3.5%) in the olmesartan arm and 94 (4.2%) in the placebo arm had at least 1 episode of diarrhea or diarrhea-associated diseases. We also observed no difference between the groups in the occurrence of any intestinal TEAE. The incidence of abdominal pain or related symptoms was also comparable (Table). In the olmesartan group, 127 patients (5.7%) experienced at least 1 episode of abdominal discomfort vs 125 (5.6%) in the placebo group. The reported incidences of fatigue and weight decrease were also similar. Furthermore, we determined whether more patients prematurely terminated study participation because of intestinal or abdominal discomfort–related TEAEs. Three patients in the olmesartan group (all 3 having diarrhea) and 3 patients in the placebo group (2 having diarrhea and 1 having gastroenteritis) stopped taking the study medication because of specific gastrointestinal findings. Eight additional patients in each of the 2 study arms stopped taking the study medication because of abdominal discomfort–associated TEAEs not specifically linked to the gastrointestinal tract.

TABLE. Gastrointestinal TEAEs Reported in the ROADMAP Database

Event	No. (%) of patients: Olmesartan, 40 mg (n=2232)	Placebo (n=2215)	*P* value
Intestinal-associated TEAE	78 (3.5)	94 (4.2)	.20
Diarrhea	51 (2.3)	52 (2.3)	
Gastroenteritis	17 (0.8)	25 (1.1)	
Colitis	1	6 (0.3)	
Enteritis	2 (0.1)	4 (0.2)	
Gastroduodenitis	4 (0.1)	2 (0.1)	
Colitis, ulcerative	2 (0.1)	2 (0.1)	
Duodenitis	2 (0.1)	2 (0.1)	
Gastrointestinal disorder	3 (0.1)	1	
Gastrointestinal infection	1	3 (0.1)	
Enteritis, infectious	0	2 (0.1)	
Abdominal discomfort–associated TEAE	127 (5.7)	125 (5.6)	.95
Abdominal pain	61 (2.7)	52 (2.3)	
Upper	26 (1.2)	24 (1.1)	
Lower	2 (0.1)	1	
Location not reported by physician	33 (1.4)	27 (1.2)	
Dyspepsia	34 (1.5)	29 (1.3)	
Nausea	30 (1.3)	34 (1.5)	
Vomiting	13 (0.6)	13 (0.6)	
Flatulence	6 (0.3)	9 (0.4)	
Abdominal discomfort	4 (0.2)	4 (0.2)	
Irritable bowel syndrome	2 (0.1)	3 (0.1)	
Epigastric discomfort	2 (0.1)	2 (0.1)	
Gastrointestinal pain	1	0	
Fatigue	25 (1.1)	20 (0.9)	
Weight decrease	17 (0.8)	11 (0.5)	

ROADMAP = Randomised Olmesartan and Diabetes Microalbuminuria Prevention; TEAE = treatment-emergent adverse event.

In summary, in more than 2200 patients taking high-dose olmesartan for more than 3 years, we did not observe an intestinal effect of olmesartan. In the ROADMAP study, we could not find a link between the occurrence of diarrhea-associated complications and the intake of 40 mg/d of olmesartan. This finding might be because spruelike enteropathy is a rare event. Indeed, the 22 reported cases in the report by Rubio-Tapia et al came from 16 different states and were diagnosed at the Mayo Clinic during a time frame of 3 years. We cannot rule out the possibility

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that in this very rare disease the intestinal renin-angiotensin system plays a role; however, our data from the ROADMAP database did not identify a link between olmesartan use and the occurrence of gastrointestinal disease.

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Potential Competing Interests: Both authors have received honoraria for lectures from Daiichi-Sankyo. Dr Haller is a medical advisor to Daiichi-Sankyo and was supported by research grants.

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3. Haller H, Viberti GC, Mimran A, et al. Preventing microalbuminuria in patients with diabetes: rationale and design of the Randomised Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study. *J Hypertens.* 2006;24(2):403-408.

http://dx.doi.org/10.1016/j.mayocp.2012.10.005

Small Bowel Histopathologic Findings Suggestive of Celiac Disease in an Asymptomatic Patient Receiving Olmesartan

To the Editor: Rubio-Tapia et al[1] recently reported a possible association of olmesartan therapy with an unexplained severe enteropathy symptomatically resembling celiac disease (CD) or sprue. The 22 patients described were seen at Mayo Clinic in the relatively short period of August 1, 2008, to August 1, 2011. The usual presentation was chronic diarrhea and weight loss, sometimes requiring hospitalization. Onset of symptoms was months to years after initiation of olmesartan treatment. Intestinal biopsy specimens from 15 patients revealed villous atrophy and variable degrees of mucosal inflammation. Five patients had evidence of colonic inflammation. Most remarkably, a gluten-free diet did not resolve symptoms, whereas both marked symptomatic improvement and resolution of histopathologic findings occurred on withdrawal of olmesartan therapy.

We describe a patient who had been taking olmesartan for 3 years at which time small bowel histopathologic findings suggesting CD were documented, but symptoms of CD enteropathy were absent. This anecdotal observation suggests the possibility that olmesartan could be associated with histopathologic findings for a substantial period before the onset of enteropathy or alternatively that such histopathologic findings might persist for years without the onset of symptoms.

A 59-year-old man experienced mild, normochromic, normocytic anemia in 2007. Workup revealed an isolated vitamin B_{12} deficiency (172 pg/mL), which was ascribed to long-term ranitidine therapy for gastroesophageal reflux and which responded to oral vitamin B_{12} supplementation at 1000 μg/d. However, the anemia did not improve. The gastrin level was 41 pg/mL (reference range, <100 pg/mL); the intrinsic factor antibody test result was negative.

Coincidentally, the patient underwent upper gastrointestinal endoscopy for symptoms consistent with worsening gastric reflux. The only macroscopic finding was nodularity in the duodenal bulb consistent with prominent Brunner glands, which was attributed to acid wash. However, a biopsy specimen from the second portion of the duodenum revealed mild expansion of the lamina propria and increased intraepithelial lymphocytes (IELs) with no significant villous blunting, suggesting (but not diagnostic of) possible CD. The patient reported no diarrhea but had occasional mild constipation. He had a first-degree cousin with CD, but no other family members were known to have CD. Findings from a workup for CD were unremarkable, including negative tissue transglutaminase antibody results (0.9 AU; reference range, <7.0 AU), normal total IgA level (127 mg/dL; reference range, 50–500 mg/dL), normal vitamin K_1 level (1.16 ng/mL; reference range, 0.10-2.10), normal prothrombin time, and negative *Helicobacter pylori* antibody results. He was HLA-DQ2 positive but HLA-DQ8 negative.

Because the findings were unusual, a repeated upper endoscopy and a colonoscopy were performed in August 2010. The small bowel gross appearance was unchanged; the colonic examination findings were unremarkable. A small bowel biopsy specimen revealed increased IELs with mild villous blunting (interpreted as unchanged from the prior study); the colonic biopsy results were normal. The tissue transglutaminase antibody test result was again negative, and the total IgA level was normal.

A stool specimen for *Giardia* and *Cryptosporidium* immunoassays, obtained because of an episode of prolonged (6 weeks' duration) diarrhea during international travel 10 years previously, produced negative results. A trial of a gluten-free diet was considered, but the patient elected not to pursue this given the absence of symptoms, the uncertain diagnosis, and the logistical difficulties of dietary adherence during frequent domestic and international travel.

Hypertension had been diagnosed in 2003, and therapy with losartan was initiated. In 2004, losartan therapy was discontinued, and olmesartan therapy, 20 mg/d, was begun. Olmesartan therapy was well tolerated, and the hypertension was well controlled. On publication of the article by Rubio-Tapia et al, olmesartan was identified as a possible cause of the unusual findings. Olmesartan therapy will be discontinued, with monitoring of vitamin B_{12} levels and consideration for repeated upper gastrointestinal endoscopy.

Although Rubio-Tapia et al are careful to avoid claiming a proven causal relationship between olmesartan therapy and the observed spruelike enteropathy, the data are highly suggestive of more than just a coincidental association. The authors posit that the long interval between initiation of olmesartan therapy and onset of symptoms of enteropathy, as observed in their patients, could be consistent with cell-mediated immunity damage. They further suggest that a potential mechanism for the enteropathy could relate to inhibitory effects of angiotensin II receptor antagonists on transforming growth factor β action because transforming growth factor β is important in gut immune homeostasis.

Another interesting observation by the authors is that 68% of their patients

Exhibit G

MAYO CLINIC

ORIGINAL ARTICLE

Olmesartan, Other Antihypertensives, and Chronic Diarrhea Among Patients Undergoing Endoscopic Procedures: A Case-Control Study

Ruby Greywoode, MD; Eric D. Braunstein, MD; Carolina Arguelles-Grande, MD; Peter H.R. Green, MD; and Benjamin Lebwohl, MD, MS

Abstract

Objective: To investigate a recent association between the use of the angiotensin receptor-blocker (ARB) olmesartan and a severe enteropathy resembling celiac disease.

Patients and Methods: We searched our endoscopy database for all outpatient esophagogastroduodenoscopy (EGD) or colonoscopy examinations in patients aged at least 50 years during the period January 1, 2007, to March 31, 2013. Cases were those whose examination indication was diarrhea, and controls were those whose examination indication was esophageal reflux (EGD) or colorectal cancer screening (colonoscopy). We compared cases with controls with regard to the proportion of those listing olmesartan among their medications. Secondary exposures were the proportion of those taking non-olmesartan ARBs or other antihypertensive medications. We also examined biopsy results to determine whether there were histologic changes associated with the use of olmesartan.

Results: We identified 2088 patients undergoing EGD and 12,428 patients undergoing colonoscopy meeting inclusion criteria. On multivariate analysis, there was no statistically significant association between olmesartan and diarrhea among those undergoing EGD (odds ratio, 1.99; 95% CI, 0.79-5.00) or colonoscopy (odds ratio, 0.63; 95% CI, 0.23-1.74). Review of pathology reports of the EGD and colonoscopy groups showed no association between the use of olmesartan and the histologic diagnosis of celiac disease (P=.61) or microscopic colitis (P=1.0), respectively.

Conclusion: Our findings suggest that neither olmesartan nor other ARBs were associated with diarrhea among patients undergoing endoscopy. The spruelike enteropathy recently associated with olmesartan is likely a rare adverse effect and milder presentations are unlikely.

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A number of recent reports in the literature have implicated olmesartan, an angiotensin II receptor-blocker (ARB) commonly prescribed for the treatment of hypertension, in the development of a severe form of chronic diarrhea and intestinal villous atrophy resembling celiac disease.[1-3] In an initial case series, 22 individuals were diagnosed with refractory celiac disease because of chronic diarrhea and villous atrophy on histology, although all lacked the diagnostic markers of celiac disease and derived no clinical improvement from a gluten-free diet.[1] These individuals were observed to be taking olmesartan and experienced significant clinical and histological improvement with the cessation of the drug, suggesting a strong association between olmesartan and the development of a severe form of spruelike enteropathy.

A recent review of individuals with villous atrophy of unclear etiology also observed that a number of those originally considered to have unclassified sprue (negative celiac disease serologies despite evidence of villous atrophy on duodenal biopsy) were taking olmesartan.[4] As in the previous study, all these patients had symptomatic improvement after the discontinuation of the drug. Similarly, a case series of patients with collagenous sprue at the Mayo Clinic reported that of 30 patients with collagenous sprue, 27% had been taking olmesartan.[5] Although the diagnosis of celiac disease is made on duodenal biopsy, the finding of microscopic colitis (lymphocytic and/or collagenous colitis) in the large intestine is associated with a diagnosis of celiac disease. Thus, a positive association between microscopic colitis and the use of olmesartan could suggest a

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spectrum of histologic changes associated with the drug. In addition, lymphocytic colitis was present in 22% of the initial case series describing olmesartan-associated spruelike enteropathy.[1]

Another recent case report described similar findings of negative serologic markers despite mild villous atrophy in a patient taking olmesartan; however, unlike the previous reports, this patient exhibited no symptoms of diarrhea, suggesting that olmesartan may produce a spectrum of disease with preclinical or asymptomatic histologic changes.[6]

It is unclear whether these cases described in the literature highlight a very rare reaction to olmesartan, or whether patients with severe disease represent the most clinically overt sample, with milder forms of olmesartan enteropathy left undetected. It is also unclear whether olmesartan alone is associated with this phenomenon or whether other members of its drug class share similar effects. We therefore performed a case-control study with the aim of investigating a possible association between diarrhea and the use of olmesartan among patients undergoing endoscopic procedures. As a secondary aim, we measured for associations between diarrhea and other antihypertensive medication exposures.

METHODS

Patients

Using an electronic endoscopy database, we identified all outpatient esophagogastroduodenoscopy (EGD) or colonoscopy examinations in patients aged at least 50 years during the 75-month period spanning the dates January 1, 2007, and March 31, 2013, at Columbia University Medical Center, a hospital-based endoscopy suite in New York City. As part of routine preendoscopy protocol, all patients were interviewed in person by a nurse and asked to provide a list of all their current medications (prescription as well as nonprescription). Cases were defined as those whose examination indication was listed as diarrhea, and controls were defined as those whose examination indication was esophageal reflux (in those undergoing EGD) or colorectal cancer screening (in those undergoing colonoscopy). We compared cases with controls with regard to the proportion of those who listed olmesartan among their medications. Secondary exposures were the proportion of those taking nonolmesartan ARBs or other antihypertensive medications. We used multivariate logistic regression, adjusting for age and sex, to quantify the association between these drug exposures and case status, that is, diarrhea.

To determine whether there were histologic changes associated with the use of olmesartan, we examined the biopsy results of both the EGD and the colonoscopy groups. We examined the upper endoscopy cases (ie, patients who presented for EGD because of diarrhea) to determine whether there were any diagnoses of celiac disease and whether there was an increased proportion of olmesartan use among those who underwent small intestinal biopsy during the procedure. To do so, we identified patients with celiac disease (either newly diagnosed or previously diagnosed) in this data set using a query for the *International Classification of Diseases, Ninth Revision* code for celiac disease (579.0) followed by manual review of the chart of each case with this diagnosis code. Using the search terms "microscopic colitis" or "lymphocytic colitis" or "collagenous colitis," we also manually reviewed the biopsy reports of colonoscopy cases (ie, patients who underwent colonoscopy because of diarrhea) to determine whether there was an increased proportion of microscopic colitis among patients taking olmesartan.

Statistical Analyses

For the primary outcome, we performed multiple logistic regression, controlling for age and sex, and calculated adjusted odds ratios (ORs) and their corresponding 95% CIs. All reported *P* values are 2-sided. We used SAS version 9.2. When comparing the use of olmesartan among cases diagnosed with celiac disease or microscopic colitis, we used the Fisher exact test. The Institutional Review Board at Columbia University Medical Center approved this study.

RESULTS

We identified 2088 patients undergoing EGD and 12,428 patients undergoing colonoscopy who met the inclusion criteria. Cases as defined by those undergoing endoscopy because of diarrhea were 393 (19%) in the EGD and 867 (7%) in the colonoscopy cohort (Table 1). Women composed 65% and 59% of the EGD and

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colonoscopy groups, respectively. Most patients were aged between 50 and 69 years (range, 50-93 y). The proportion of patients taking any antihypertensive was 46% (968/2088) of the patients in the EGD group and 42% (5267/12428) of the patients in the colonoscopy group. The use of olmesartan in particular was reported by 22 (1%) of the EGD and 83 (0.7%) of the colonoscopy study patients, while use of nonolmesartan ARB was reported by 228 (11%) of the EGD and 1048 (8%) of the colonoscopy patients.

Univariate (Table 2) and multivariate (Table 3) analyses demonstrated that there was no statistically significant association between the use of olmesartan and diarrhea among those undergoing EGD (multivariate OR, 1.99; 95% CI, 0.79-5.00) or colonoscopy (multivariate OR, 0.63; 95% CI, 0.23-1.74). Associations that reached statistical significance on multivariate analysis were an increased risk of diarrhea with older age (EGD OR for ≥70 y vs 50-59 y, 1.35; 95% CI, 1.01-1.80; colonoscopy OR, 2.22; 95% CI; 1.86-2.65) and female sex (EGD OR, 1.48; 95% CI, 1.16-1.90; colonoscopy OR, 1.69; 95% CI, 1.45-1.97). In addition, there was a decreased risk of diarrhea among EGD patients taking calcium channel blockers (OR, 0.61; 95% CI, 0.38-0.98) and angiotensin-converting enzyme inhibitors (OR, 0.67; 95% CI, 0.50-0.92) as well

TABLE 1. Characteristics of Study Patients[a,b]

Characteristic	EGD (n=2088)	Colonoscopy (n=12,428)
Age (y)		
50-59	779 (37)	5621 (45)
60-69	763 (37)	4141 (33)
70+	546 (26)	2666 (21)
Sex		
Female	1364 (65)	7387 (59)
Male	724 (35)	5041 (41)
Procedure indication		
Diarrhea (cases)	393 (19)	867 (7)
Reflux (controls)	1695 (82)	-
CRC Screening (controls)	-	11,561 (93)
HTN medications		
None	1120 (54)	7161 (58)
Any	968 (46)	5267 (42)
Olmesartan	22 (1)	83 (0.7)
Any ARB	228 (11)	1048 (8)
Any ACEI	418 (20)	2235 (18)
HCTZ/chlorthalidone	218 (10)	1539 (12)
Beta blocker	404 (19)	2245 (18)
Calcium channel blocker	171 (8)	921 (7)

[a]ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor-blocker; CRC = colorectal cancer; EGD = esophagogastroduodenoscopy; HCTZ = hydrochlorothiazide; HTN = hypertension.
[b]Values are No. (percentage).

TABLE 2. Univariate Analysis of Factors Associated With Diarrhea[a,b]

Factor	EGD			Colonoscopy		
	Diarrhea	Control	*P*	Diarrhea	Control	*P*
Age (y)			.38			<.001[c]
50-59	139 (18)	640 (82)		290 (5)[c]	5331 (95)[c]	
60-69	140 (18)	623 (82)		297 (7)[c]	3844 (93)[c]	
70+	114 (21)	432 (79)		280 (11)[c]	2386 (89)[c]	
Sex						
Female	285 (21)[c]	1079 (79)[c]	<.001[c]	608 (8)	6779 (92)[c]	<.001[c]
Male	108 (15)	616 (85)		259 (5)	4782 (95)	
Any antihypertensive	158 (16)[c]	810 (84)[c]	.006[c]	369 (7)	4898 (93)	.91
No antihypertensive	235 (21)	885 (79)		498 (7)	6663 (93)	
Olmesartan	7 (32)	15 (68)	.12	4 (5)	79 (95)	.44
Any ARB	34 (15)	194 (85)	.11	87 (8)	961 (92)	.08
Any ACEI	60 (14)[c]	358 (86)[c]	.009[c]	142 (6)	2093 (94)	.20
HCTZ/chlorthalidone	34 (16)	184 (84)	.20	84 (5)	1455 (95)[c]	.01[c]
Beta blocker	74 (18)	330 (82)	.77	175 (8)	2070 (92)	.09
Calcium channel blocker	22 (13)[c]	149 (87)[c]	.04[c]	66 (7)	855 (93)	.81

[a]ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor-blocker; EGD = esophagogastroduodenoscopy; HCTZ = hydrochlorothiazide.
[b]Values are No. (percentage).
[c]Exposures meeting statistical significance.

TABLE 3. Multivariate Analysis of Factors Associated With Diarrhea[a]

Factor	EGD		Colonoscopy	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (y)				
50-59	1.0	-	1.0	-
60-69	1.12 (0.86-1.45)	.41	1.44 (1.22-1.71)[b]	<.001[b]
70+	1.35 (1.01-1.80)[b]	.04[b]	2.22 (1.86-2.65)[b]	<.001[b]
Sex				
Female	1.48 (1.16-1.90)[b]	.002[b]	1.69 (1.45-1.97)[b]	<.001[b]
Male	1.0	-	1.0	-
Any antihypertensive	0.72 (0.57-0.90)[b]	.005[b]	0.90 (0.76-1.04)	.14
Olmesartan	1.99 (0.79-5.00)	.14	0.63 (0.23-1.74)	.37
Any ARB	0.73 (0.49-1.09)	.12	1.17 (0.92-1.49)	.20
Any ACEI	0.67 (0.50-0.92)[b]	.01[b]	0.89 (0.73-1.08)	.23
HCTZ/chlorthalidone	0.87 (0.58-1.30)	.49	0.66 (0.51-0.84)[b]	<.001[b]
Beta blocker	1.07 (0.80-1.43)	.66	1.11 (0.93-1.33)	.25
Calcium channel blocker	0.61 (0.38-0.98)[b]	.04[b]	0.97 (0.75-1.27)	.84

[a]ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor-blocker; EGD = esophagogastroduodenoscopy; HCTZ = hydrochlorothiazide.
[b]Exposures meeting statistical significance.

as among colonoscopy patients taking thiazide diuretics (OR, 0.66; 95% CI, 0.51-0.84).

Of the 393 patients who presented for upper endoscopy because of diarrhea, 70 (18%) had biopsy results consistent with celiac disease and 2 (0.5%) of those were taking olmesartan. When compared with EGD patients who presented because of diarrhea without a diagnosis of celiac disease on biopsy, there was no statistically significant association between the use of olmesartan and the diagnosis of celiac disease (*P*=.61) (Table 4).

Of the 867 patients who presented for colonoscopy because of diarrhea, 762 (88%) underwent biopsy and 59 of these had a diagnosis of microscopic colitis. None of the diagnoses of microscopic colitis, however, was associated with current use of olmesartan (Table 5). When compared with colonoscopy cases without a diagnosis of microscopic colitis on biopsy, there was no statistically significant association between the use of olmesartan and the diagnosis of microscopic colitis (*P*=1.0).

TABLE 4. Antihypertensive Use in EGD Cases With/Without Diagnosis of Celiac Disease on Biopsy[a,b]

Antihypertensive	Diagnosis celiac disease (n=70)	No diagnosis celiac disease (n=323)
HTN medication, any	23 (33)	135 (42)
Olmesartan[c]	2 (3)	5 (2)
Any ARB	2 (3)	32 (10)
Any ACEI	11 (16)	49 (15)
HCTZ/chlorthalidone	7 (10)	27 (8)
Beta blocker	10 (14)	64 (20)
Calcium channel blocker	2 (3)	20 (6)

[a]ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor-blocker; HCTZ = hydrochlorothiazide; HTN = hypertension.
[b]Values are No. (percentage).
[c]*P*=.61.

DISCUSSION

In this case-control study, we sought to examine the recently described association between the use of olmesartan and chronic severe diarrhea using a large sample of patients presenting for endoscopy at a tertiary referral medical center. Previous data on the risk of diarrhea among individuals taking olmesartan come from the original trial comparing the use of olmesartan to placebo in patients with diabetes. Data from that trial suggested no increased gastrointestinal adverse effects of the drug; however, the risk of diarrhea with the use of olmesartan was not a primary end point of the study.[7] To our knowledge, this is the first study to compare the rate of use of olmesartan and biopsy findings in patients with symptomatic chronic diarrhea vs asymptomatic individuals presenting for endoscopic evaluation.

We found that neither olmesartan nor other ARBs were associated with diarrhea among patients undergoing endoscopy. Other antihypertensives were negatively associated with diarrhea, possibly as a result of their known constipating effects. Analysis of the biopsy results of those patients who presented for endoscopy because of diarrhea similarly resulted in negative findings: there was no statistically significant association between patients whose biopsy results were consistent with a diagnosis of celiac disease or microscopic colitis and the use of olmesartan. Notably, most of the individuals in the initial case series who developed sprue-like enteropathy associated with the use of olmesartan were HLA DQ2 or DQ8 positive, suggesting potential predisposing factors in certain individuals; however, the underlying mechanism remains unknown.

Strengths of this study include the large sample size as well as the comprehensive and protocoled, direct, in-person solicitation of home medication use immediately preceding each endoscopic procedure. Limitations of this study include its retrospective nature, although it examines a large sample size for a rare event

that may not be amenable to a prospective design. There was also a relatively small prevalence of use of olmesartan (0.7%-1%) among study patients, limiting the power of this analysis. Because the upper bound of our 95% CI was 5.00 in the EGD analysis and 1.74 in the colonoscopy analysis, a meaningful association between olmesartan and diarrhea may exist that was not detectable because of the relative rarity of use of olmesartan.

CONCLUSION

Our findings suggest that the spruelike enteropathy recently associated with olmesartan is a rare event and milder presentations causing diarrhea among substantial numbers of outpatients are unlikely. Future studies should focus on the mechanisms by which olmesartan causes severe spruelike enteropathy, and the identification of patient-related risk factors that predispose for this rare but serious outcome.

Abbreviations and Acronyms: ARB = angiotensin receptor-blocker; **EGD** = esophagogastroduodenoscopy; **OR** = odds ratio

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TABLE 5. Antihypertensive Use in Colonoscopy Cases With/Without Microscopic Colitis on Biopsy[a,b]

Antihypertensive	Microscopic colitis (n=59)	No microscopic colitis (n=703)
HTN medication, any	24 (41)	296 (42)
Olmesartan[c]	0 (0)	4 (0.6)
Any ARB	5 (8)	71 (10)
Any ACEI	13 (22)	109 (16)
HCTZ/chlorthalidone	6 (10)	63 (9)
Beta blocker	8 (14)	137 (19)
Calcium channel blocker	2 (3)	53 (8)

[a]ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor-blocker; HCTZ = hydrochlorothiazide; HTN = hypertension.
[b]Values are No. (percentage).
[c]$P=1.0$.

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Exhibit H

Sprue-like histology in patients with abdominal pain taking olmesartan compared with other angiotensin receptor blockers

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ABSTRACT

Aims A severe syndrome characterised by life-threatening diarrhoea and severe sprue-like histology has been described in patients taking the angiotensin receptor blocker (ARB) olmesartan. It is unknown whether there are any histopathological changes in patients without severe diarrhoea exposed to this medication. It is also unknown whether other ARBs cause sprue-like histology.

Methods Retrospective cohort study of patients with abdominal pain undergoing upper gastrointestinal endoscopy with duodenal biopsy who were taking ARBs. Patients taking olmesartan (n=20) and a non-olmesartan ARB (n=20) were compared with age and sex-matched controls. Histological features (classic sprue-like and other inflammatory changes) were analysed.

Results No single histopathological finding was significantly more common in olmesartan-using patients than controls. However, 10 of 20 olmesartan patients had one or more sprue-like histological features compared with 4 of 20 age-matched and sex-matched controls not taking ARBs (p=0.10). Patients taking ARBs other than olmesartan were not more likely than controls to have one or more of these sprue-like histological features (9/20 vs. 12/20, p=0.34).

Conclusions There were no statistically significant differences between olmesartan users with abdominal pain and controls for any single histopathological abnormality. However, there were trends towards significance for individual abnormalities as well as for a composite outcome of sprue-like changes. This raises the possibility that there is a spectrum of histological changes associated with olmesartan use.

INTRODUCTION

Olmesartan medoxomil is a commonly used antihypertensive medication, which acts by blocking angiotensin receptors. Recently, a series of cases were described in which 22 patients presented with debilitating diarrhoea and had a sprue-like enteropathy on histological examination due to olmesartan. The diarrhoea was so severe that 14 patients required hospitalisation and 4 required total parenteral nutrition. Serological testing for coeliac disease was negative in all cases and none improved with a gluten-free diet. All had biopsies, which showed severe sprue-like changes (villous atrophy, lamina propria inflammation and intraepithelial lymphocytosis (IEL)). Seven of the patients had collagenous sprue. All patients had dramatic improvement, with resolution of their diarrhoea following cessation of olmesartan.[1] As a major referral centre for coeliac disease, we have subsequently encountered a number of such cases and several other case series and reports have been published, which demonstrate similar clinical and histopathological findings.[2–12] At present, this adverse drug reaction is thought to be a rare occurrence. A recent case–control study did not show an association between olmesartan use and chronic diarrhoea in patients presenting for oesophagogastroduodenoscopy (OGD) or colonoscopy.[13]

While it is unusual to encounter severe villous atrophy in non-coeliac patients, milder changes which may overlap with sprue-like enteropathies (such mild or focal IEL) are common.[2 14] Medication reactions, particularly non-steroidal anti-inflammatory drugs, are commonly listed in the differential of such pathological findings.[15] Other drugs also enter the differential, but it is unknown whether olmesartan exposure should be considered when encountering such findings. It is also unknown whether other angiotensin receptor blockers (ARBs) may cause histopathological changes.

Because it is unclear whether the severe sprue-like enteropathy seen in a few patients taking olmesartan is the severe end of a spectrum of intestinal injury, we identified patients taking olmesartan who had undergone endoscopy for abdominal pain with duodenal biopsy and systematically studied the biopsies. We also identified patients with abdominal pain taking other ARBs who had duodenal biopsy and examined their biopsies to determine whether the changes were specific for olmesartan. We identified those patients whose indication for the procedure was abdominal pain to avoid those whose symptom was diarrhoea.

METHODS

We performed a retrospective cohort study using the electronic medical record of Columbia University Medical Center endoscopy unit (ProVation Medical Systems, Wolters Kluwer Health, New South Wales, Australia). This record includes all home medication use reported by outpatients undergoing OGD. This list of medications is ascertained by a trained nurse during an interview immediately preceding the procedure. We queried the medical record for patients in whom the indication for OGD was abdominal pain (self-reported, no formal diagnostic criteria employed) and identified 20 outpatients who listed olmesartan as one of their medications. We then matched each patient by age and gender to a control patient who did not report any ARB when listing his/her medications. Using the same process, we identified

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another 20 users of non-olmesartan ARBs and corresponding matched controls. We excluded all patients with a history of coeliac disease, inflammatory bowel disease or *Helicobacter pylori* infection (present or prior). In total, we identified 80 patients undergoing OGD for abdominal pain: 20 olmesartan users with 20 matched controls and 20 non-olmesartan ARB users with 20 matched controls. This study was approved by the Columbia University Medical Center Institutional Review Board.

Abnormalities that are seen in enteropathies that include coeliac disease and the sprue-like enteropathy of olmesartan including villous atrophy, crypt hyperplasia, increased IEL concentration, chronic lamina propria inflammation and increased subepithelial collagen deposition were evaluated on routine H&E-stained slides by a gastrointestinal pathologist who was blinded to the medication status (SML). The maximum IEL count in 100 epithelial cells was counted by routine H&E stain. In addition, increased crypt apoptosis (abnormal was considered more than 2 crypt apoptotic bodies in any 10 consecutive crypts or more than one apoptotic body per biopsy piece), active inflammation (defined as any extravascular neutrophils) and eosinophilia were also documented.

Statistical analysis

We compared the prevalence of each of the above histopathological findings among ARB users and their matched controls. We used the χ^2 and Fisher exact test when comparing proportions, and used the Mann–Whitney test when comparing IEL counts. After reviewing these comparisons, we subsequently performed a post-hoc analysis comparing ARB-exposed subjects with controls with regard to the composite outcome of one or more of the following findings: architectural abnormalities (villous atrophy or crypt hyperplasia), increased IEL or chronic inflammation. In this analysis, individuals who met one or more of these aforementioned criteria were collectively compared, via χ^2 testing, to those who met none of these criteria.

All p values reported are two-sided. We used SAS V9.3 (Cary, North Carolina, USA) for statistical calculations.

RESULTS

Among the 20 olmesartan users, the mean age was 59.5 years and 70% were women (table 1).

Among 20 non-olmesartan ARB users, the mean age was 58.5 years and 55% were women. The indication for OGD was abdominal pain in all cases and controls. When we compared duodenal biopsies of olmesartan users with controls, we identified no single histopathological finding that was significantly more frequent in either group (table 2).

However, there were variables and a composite outcome which showed trends towards significance. Of note, 10 of 20 olmesartan-exposed patients (50%) had one or more of the following sprue-like features: architectural distortion (villous atrophy and/or crypt hyperplasia), generalised increase in IEL and chronic inflammation (figure 1A–C). This compares with 4 of 20 control patients (10%, p=0.10). Regarding individual findings, olmesartan users had more positive findings than control patients for each variable investigated (other than increased subepithelial collagen which was not seen in any case or control), though none achieved statistical significance. Specifically, 25% of olmesartan users had foci of villous atrophy compared with 6% of control patients (p=0.33). The mean maximum IEL count was 13.7 in the olmesartan group compared with 10.6 for controls (p=0.09). Certain other features also were more common in olmesartan users than in control patients, but they too failed to reach statistical significance. The most notable of these was increased crypt apoptosis, which was seen in 25% of olmesartan users compared with 10% of controls (figure 1D).

We also compared duodenal biopsies from individuals taking ARBs other than olmesartan with patients taking no ARB. There were no statistically significant differences and no trends that suggested a similar effect (table 2).

DISCUSSION

Olmesartan is a widely prescribed ARB used in the management of hypertension. Rarely, patients taking this drug develop a life-threatening diarrheal illness with duodenal biopsies that reveal a severe enteropathy often with increased collagen deposition.[1] A study performed at our institution showed that over 10 years, 72 patients had been referred with a diagnosis of seronegative villous atrophy (negative coeliac disease serologies). The most common diagnosis in this group was seronegative coeliac disease (20 patients who had coeliac disease associated human leucocyte antigen haplotypes and responded to a gluten-free diet). The second most common diagnosis (n=19) was medication-related enteropathy. Sixteen patients had olmesartan exposure and had similar clinical and histological findings as described in the Mayo Clinic series. Eleven of the 16 olmesartan-exposed patients had increased subepithelial collagen.[2] Of considerable relevance to our study is a case reported by Talbot. The patient described was taking olmesartan, but did not have diarrhoea (presented with constipation). The patient had multiple endoscopies with biopsy. The first duodenal biopsy showed normal duodenal architecture

Table 1 Patient characteristics

	Olmesartan analysis		Other ARB analysis	
	Olmesartan users (n=20)	Matched controls (n=20)	Other ARB users (n=20) Losartan: 11 Valsartan: 3 Telmisartan: 3 Irbesartan: 2 Candesartan: 1	Matched controls (n=20)
Age (median, range)	59.5 (48–76)	59.5 (48–76)	58.5 (35–84)	58.5 (35–84)
Gender				
Male	6 (30)	6 (30)	9 (45)	9 (45)
Female	14 (70)	14 (70)	11 (55)	11 (55)

ARB, angiotensin receptor blocker.

Table 2 Histological features of olmesartan and other ARB users compared with controls

	Olmesartan analysis			Other ARB analysis		
	Olmesartan users (n=20) (%)	Matched controls (n=20) (%)	p Value	Other ARB users (n=20) (%)	Matched controls (n=20) (%)	p Value
Villous atrophy	4/16 (25)*	1/16 (6)	0.33	1/14 (7)*	2/19 (11)	1.0
Crypt hyperplasia	4/16 (25)*	2/17 (12)	0.40	3/14 (21)*	4/18 (22)	1.0
Mean maximum IEL count	13.7	10.6	0.09	13.0	18.5	0.35
Generalised IEL increase	4/20 (20)	2/20 (10)	0.67	2/20 (10)	6/20 (30)	0.24
Chronic inflammation	5/20 (25)	2/20 (10)	0.40	7/20 (35)	6/20 (30)	1.0
Eosinophilia	2/20 (10)	0/20 (0)	0.49	3/20 (15)	2/20 (10)	1.0
Neutrophilia	8/20 (40)	6/20 (30)	0.74	4/20 (20)	7/20 (35)	0.48
Increased crypt apoptosis	5/20(25)	2/20 (10)	0.40	6/20 (30)	8/20 (40)	0.74
One or more sprue-like features (architectural abnormalities, generalised increased IEL, chronic inflammation)	10/20 (50)	4/20 (20)	0.10	9/20 (45)	12/20 (60)	0.34

*Villous atrophy and crypt hyperplasia was not evaluated in 4 olmesartan cases and in 6 ARB cases due to poor orientation.
ARB, angiotensin receptor blocker; IEL, intraepithelial lymphocyte.

but had increased lamina propria lymphoplasmacytic inflammation and IEL. A subsequent biopsy was similar, although showed 'mild villous blunting.' Based on the reports previously described, this patient was taken off olmesartan despite the lack of significant symptoms.[16] It is intriguing to consider whether this patient would have developed the 'full-blown' clinical and histological syndrome if he had continued to take this agent. Also of particular relevance to this study is a case, which showed similar clinical and pathological characteristics as were described in the Mayo series of olmesartan patients in a patient taking another ARB, valsartan.[17]

To determine whether olmesartan usage was associated with intestinal damage, short of the severe sprue-like enteropathy, we identified patients with abdominal pain who were taking olmesartan or other ARBs and had a duodenal biopsy. We demonstrated a trend towards sprue-like enteropathic changes in individuals taking olmesartan compared with controls. The trend towards increased crypt apoptosis is interesting mechanistically, as certain other drugs known to cause intestinal damage often demonstrate this finding (e.g. mycophenolate mofetil).[18] These changes appear to be specific for olmesartan as there were none identified in those taking other ARBs.

This is the first study to our knowledge that investigates whether exposure to olmesartan or other ARBs is associated with histopathological abnormalities among outpatients

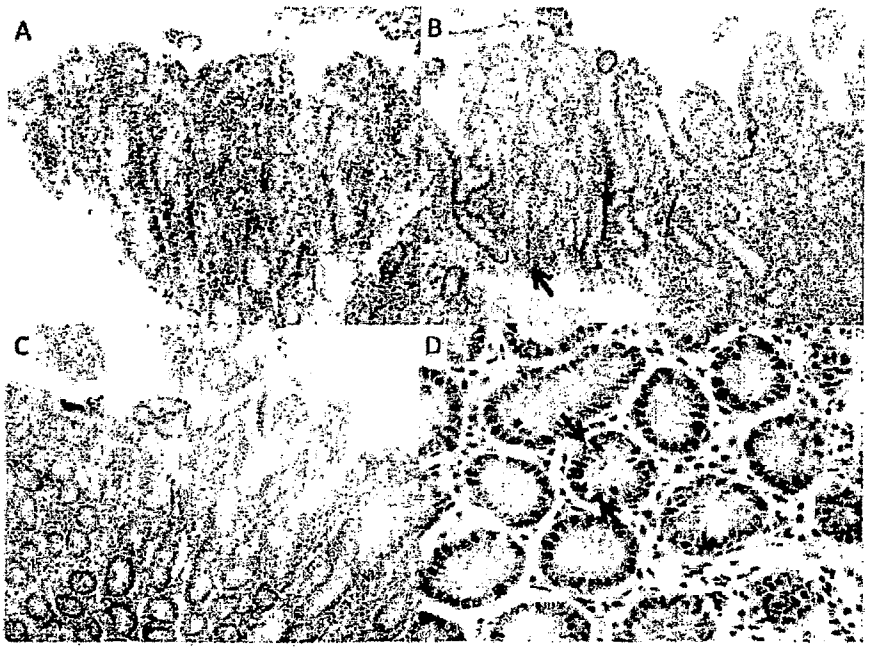

Figure 1 Highlighted findings in olmesartan users. (A) Representative photomicrograph of a small bowel biopsy from an individual showing one of several foci of villous atrophy, this particular case shows total villous atrophy but lacks intraepithelial lymphocytosis (H&E 200×). (B) A case with milder findings, including mild villous atrophy and focally pronounced crypt hyperplasia (arrow; H&E 100×). (C) This case had normal architecture, but a mild, generalised increase in intraepithelial lymphocytes (H&E 200×). (D) The case depicted in panel C also showed increased crypt apoptosis, including a crypt with 3–4 apoptotic bodies (arrows; H&E 600×).

undergoing duodenal biopsy. Our study has several limitations including its retrospective design, single centre setting and lack of information regarding duration of ARB use. We did not systematically exclude patients with known microscopic colitis; however, a post-hoc review showed that only 1 of 80 patients had microscopic colitis in our records (olmesartan user with no histopathological findings in our study). A larger sample size may have been useful, as it is possible that olmesartan causes a true increase in duodenal histopathological abnormalities but that our study was underpowered to detect this effect. Finally, we do not know whether any of the patients has subsequently discontinued olmesartan, and if so, if their abdominal pain has resolved.

This study raises the possibility that there may be a spectrum of injury associated with olmesartan use, apart from the severe syndrome that causes life-threatening diarrhoea. Further studies are needed to determine whether olmesartan use is associated with abdominal pain or other gastrointestinal symptoms and signs, as opposed to the well-characterised diarrhoea with sprue-like enteropathy. Future studies should follow-up the patients in this study to determine whether any of the olmesartan-exposed patients develop the severe enteropathic phenotype and if any of the histopathological variables we investigated are predictive thereof.

Take home messages

- This study raises the possibility that there is a spectrum of duodenal injury associated with olmesartan use.
- Angiotensin receptor blockers other than olmesartan are not associated with any histopathological findings in duodenal biopsies of patients with abdominal pain.
- Further studies are needed to determine whether olmesartan use is associated with abdominal pain and if the patients with the histopathological findings described here are at risk for developing the recently described severe sprue-like enteropathy.

Contributors SML: concept development, data collection, drafter of manuscript and guarantor of data. EDB: data collection and manuscript review. CA-G: concept development and manuscript review. GB: concept development and manuscript review. PG: concept development and manuscript review. BL: concept development, data analysis (statistics) and manuscript review.

Competing interests None.

Ethics approval Columbia University Medical Center Institutional Review Board.

Provenance and peer review Not commissioned; externally peer reviewed.

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Exhibit I

Comparative Effectiveness of Olmesartan and Other Angiotensin Receptor Blockers in Diabetes Mellitus

Retrospective Cohort Study

Raj Padwal, Mu Lin, Mahyar Etminan, Dean T. Eurich

Abstract—Olmesartan has been linked with increased risk of cardiovascular mortality and sprue-like enteropathy. We compared outcomes between olmesartan and other angiotensin receptor blockers in a large clinical registry of patients with diabetes mellitus. A retrospective cohort analysis using nationwide US-integrated insurance and laboratory claims was performed in 45 185 incident diabetic angiotensin receptor blocker users, including 10 370 (23%) olmesartan users. Hazard ratios were computed using time-dependant Cox models adjusted for sociodemographic characteristics, comorbidities, laboratory data, drug use, healthcare utilization, and the propensity to receive olmesartan. Blood pressure data were unavailable. Subjects were followed up for 116 721 patient-years. The primary end point was all-cause hospitalization or all-cause mortality and occurred in 10 915 (24%) patients. Average age was 54.3±9.6 years, 52% were men, 17% had cardiovascular disease, and 10% chronic kidney disease. Compared with other angiotensin receptor blockers, the adjusted hazard for olmesartan was 0.99 (95% confidence interval, 0.94–1.05) for all-cause hospitalization and mortality; 0.90 (0.62–1.30) for all-cause mortality; 0.99 (0.94–1.05) for all-cause hospital admission; 0.88 (0.78–1.00) for cardiovascular disease–related admission, and 1.09 (0.98–1.20) for gastrointestinal disease–related hospitalization in the overall cohort. Olmesartan use was associated with an adjusted hazard for the primary outcome of 1.11 (0.99–1.24) in subjects with history of cardiovascular disease and 1.21 (1.04–1.41) in subjects with chronic kidney disease. In conclusion, there is no robust signal for harm with olmesartan use. Risk may be increased in kidney disease; thus, given the widespread availability of alternate agents, olmesartan should be used with caution in this subgroup pending further study. (***Hypertension***. **2014;63:977-983.)** • **Online Data Supplement**

Key Words: angiotensin receptor antagonists ■ cardiovascular diseases ■ comparative effectiveness research ■ hospitalization ■ mortality ■ olmesartan

Olmesartan, an angiotensin II type 1 receptor antagonist (ARB) first approved in 2002, is commonly used for the treatment of hypertension.[1] Despite being the seventh ARB approved by the Food and Drug Administration and despite a lack of hard outcome trial data supporting its use, olmesartan is widely prescribed, with estimated worldwide sales of 2 billion US dollars in 2009.[2] Two placebo-controlled randomized controlled trials examining the efficacy of olmesartan in delaying onset/progression of renal disease in patients with diabetes mellitus, Randomized Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) and Olmesartan Reducing Incidence of End Stage Renal Disease in Diabetic Nephropathy (ORIENT), have been recently published.[3,4] In both trials, cardiovascular mortality was increased in subjects randomized to olmesartan treatment. In ROADMAP, cardiovascular deaths occurred in 15 (0.7%) olmesartan-treated subjects and 3 (0.1%) placebo-treated subjects (P=0.01). In subjects with pre-existing cardiovascular disease taking olmesartan, 11 cardiovascular deaths occurred compared with 1 in subjects assigned to placebo. In ORIENT, 10 (3.5%) subjects receiving olmesartan died of cardiovascular causes compared with 3 (1.1%) placebo-treated subjects (P>0.05). Although these data raise concerns, they do not definitively prove harm because cardiovascular death was not a primary end point, the absolute number of cardiovascular events was low in both studies, and nonfatal cardiovascular events were not significantly different between study arms in ROADMAP (81 [3.6%] for olmesartan versus 91 [4.1%] for placebo; P=0.31).

After undertaking a safety review of olmesartan in 2011, the US Food and Drug Administration determined that the benefits of the drug outweighed its potential risks in patients with hypertension but advised against use of olmesartan for

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delaying or preventing renal disease and underscored the need for more postmarketing surveillance.[5] In 2013, following case reports describing a potential association between olmesartan and sprue-like enteropathy, the Food and Drug Administration issued a second warning and announced plans to conduct further safety reviews.[6]

The objective of this study was to provide further postmarketing assessment of the comparative effectiveness and safety of olmesartan. Specifically, we assessed the effect of olmesartan therapy compared with other ARBs on overall mortality and cause-specific hospitalization and sought to quantify absolute event rates. Given prior evidence, we hypothesized that olmesartan use would increase the risk of mortality or hospitalization relative to other ARBs in patients with diabetes mellitus, and that this risk increase would be highest in patients with pre-existing cardiovascular disease and chronic kidney disease (CKD; ie, high-risk subgroups).

Methods

We performed a population-based retrospective cohort study using an anonymized large US claims and integrated laboratory database containing information on employed, commercially insured patients with dependants from all 50 states (Clinformatics Data Mart, Optum, Life Sciences). The database has been used in multiple previous studies, contains >13 million annual lives.[7–10] We analyzed patient-level, clinically rich, deidentified longitudinal data, including administrative and demographic information (sex, age, type of insurance plan, eligibility date, and income); billable medical service inpatient, outpatient, and medical procedure claims (deidentified physician and facility identifier, date and place of service, cost of service, admission and discharge dates, procedure, and diagnosis codes); and laboratory test results and pharmacy claims data (deidentified prescribing physician, drug dispensed based on national drug codes, quantity and date dispensed, drug strength, days' supply, and cost of service). *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) clinical and procedure codes were used, and data were cleaned and analyzed using protocols compliant with the Health Insurance Portability and Accountability Act.

Research ethics review board approval to conduct this study was obtained from the University of Alberta and the New England Institutional Review Board. The procedures followed were in accordance with institutional guidelines.

Cohort Selection

An inception cohort of 114 010 new ARB users with diabetes mellitus aged ≥20 years and identified between January 1, 2004 and December 31, 2009 was created. The date of the first ARB prescription was designated as the index date. New users were individuals who did not have a prior prescription claim for any ARB for ≥1 year before their index date. We limited inclusion to subjects with ≥1 year of baseline data enrolled in a commercial medical insurance plan (Figure 1). Subjects were followed up until death, termination of medical insurance, or December 31, 2010 (study end) providing a maximum follow-up of 6 years. A priori, we decided to exclude users who crossed over from olmesartan to another ARB (or vice versa) during the follow-up period (n=3257). Mortality was ascertained by linking to the US national death index file.[11] This is a highly valid and reliable method, with >98% sensitivity when social security number data are available.[12]

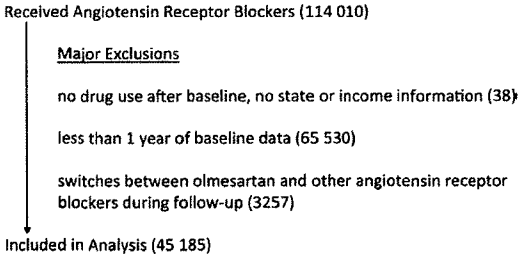

Figure 1. Inclusions and exclusions.

The primary outcome was all-cause hospital admission or death. This composite outcome was analyzed using time-to-first event (eg, either admission date or date of death) as the dependent variable. Each component of this composite end point was also analyzed separately. Cause-specific mortality was not available. Other secondary end points included cardiovascular-related hospital admissions (*ICD-9-CM* codes 410, 411.1, 428, 430–438), the combined end point of cardiovascular-related hospital admission or all-cause mortality, gastrointestinal-related hospital admissions (*ICD-9-CM* codes 530–579), and admissions related to noninfective enteritis and colitis (*ICD-9-CM* codes 555–558). Patients were censored if they did not have an outcome of interest and reached study end (December 31, 2010) or their insurance was terminated.

Analyses

Time-varying Cox proportional hazards regression was used to estimate the effect of exposure to olmesartan (relative to all other ARBs) on each outcome. Time zero was set at index date.[13] The days' supplied field in the prescription drug dispensations database was used as a proxy for the expected duration of each prescription and was used to compute time-varying drug exposure.[14] We assumed that subjects were exposed to the drug of interest unless prescription refills were not obtained for 2 consecutive days' supplied periods. If drug discontinuation occurred, subjects were classified as unexposed from the end of the first consecutive days' supplied period to the end of the study or until they restarted the drug. In this time-varying primary analysis, outcome events were attributed to a given drug if the event occurred while the subject was exposed; no legacy or carryover effects from remote exposure were assumed.

Covariates

In addition to using time-varying exposure models to limit potential bias, additional potential confounders were included in the Cox regression models as time fixed baseline variables. These included age, sex, socioeconomic status (type of medical insurance and median household income according to the 2010 US census),[15] cardiovascular comorbidities, clinical laboratory data (glycohemoglobin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, estimated glomerular filtration rate [according to the Modified Diet in Renal Disease calculation: ≥90, 89.9–60, 59.9–30, <30 mL/min], albuminuria, and hemoglobin concentrations), and prescription drugs (eg, antidiabetic agents, antiplatelet drugs, anticoagulants, statins, calcium channel blockers, β-blockers, angiotensin-converting enzyme inhibitors, renin inhibitors, diuretics, and nitrates). For patients who did not have specific clinical laboratory data measured, we used the missing indicator approach for all analyses.[16]

To further control for baseline comorbidity and illness, we included an Adjusted Clinical Groups score in the model. This single comorbidity score is derived from the Johns Hopkins Adjusted Clinical Groups score system (Version 9)[17] and is weighted by 32 adjusted diagnostic groups. It performs equally to or better than the Charlson and Elixhauser comorbidity scores.[18] In addition, we adjusted for the total number of hospital admissions in the year before the index date, the total number of chronic conditions at baseline, frailty (any occurrence of malnutrition, abnormal weight loss, morbid obesity, dementia, falls, and decubitus ulcer),[17] and the time-varying propensity to receive olmesartan. For the latter, we computed the updated propensity or probability of receiving olmesartan every 3 months throughout the follow-up period.[19] This propensity score was entered into the model as a continuous probability score that was based on ≈60 variables, including demographic variables (age, sex, age–sex interaction, state, and type of insurance), socioeconomic factors (income), comorbidities, health service use, laboratory data, markers of frailty, and drug treatments. A full list of model covariates and variables included in the propensity score is available on request.

Subgroup and Sensitivity Analyses

Subgroup analyses were performed in subjects with a baseline history of cardiovascular disease and with CKD (defined as an estimated glomerular filtration rate <60 mL/min). A sensitivity analysis in which we repeated primary analysis comparing olmesartan with all other ARBs but censored subjects who switched from one ARB class to another (instead of excluding them) was also performed.

A dose–response analysis and an analysis comparing olmesartan with individual ARBs were also performed. Further methodological details are provided in the online-only Data Supplement.

Results

Of 114 010 ARB users, the final cohort comprised 45 185 subjects (Figure 1). Mean age was 54.3 (SD, 9.6) years, 52% were men, 17% had a history of cardiovascular disease, 13% had diabetes mellitus–related complications, and 10% had CKD (Table 1). We identified 10 370 (23%) olmesartan users and 34 815 (77%) who used other ARBs during the follow-up period. Additional baseline characteristics of the study population are summarized in Table 1. The prevalence of concomitant comorbidities was either equal between groups or lower in olmesartan users compared with users of other ARBs. One exception was hypertension, which was more common in olmesartan users. The average daily ARB doses prescribed during the follow-up period were olmesartan 22.1 mg, losartan 52.1 mg, valsartan 110.5 mg, telmesartan 41.9 mg, eprosartan 424.2 mg, irbesartan 145.9 mg, and candesartan 14.1 mg.

Subjects were followed up for 116 721 patient-years (median duration, 2.3 years [interquartile range, 1.1–3.8 years]). The primary composite end point occurred in 10 915 (24%) subjects; 10 836 (24%) subjects experienced ≥1 hospital admission and 458 (1%) died (Table 2).

The crude incidence rates of all-cause hospital admission or all-cause mortality were lower in olmesartan users compared with other ARBs (Table 2). However, after time-varying, multivariable adjustment was performed, the relative hazard of the primary composite end point was similar in olmesartan users (adjusted hazard ratio [aHR], 0.99; 95% confidence interval, 0.94–1.05; Table 2; Figure 2). In addition, compared with other ARB users, aHRs in olmesartan users were 0.90 (0.62–1.30) for all-cause mortality; 0.99 (0.94–1.05) for all-cause hospital admission; and 0.88 (0.78–1.01) for cardiovascular disease–related hospitalization (Table 2).

The covariate-aHR of gastrointestinal disease–related hospitalization was 1.09 (0.98–1.20) for olmesartan users compared with other ARB users and the aHR for admissions related to noninfective enteritis and colitis was 1.21 (0.87–1.69; Table 2).

Subgroup Analyses

Results in high-risk subjects are summarized in Table 3. In subjects with pre-existing cardiovascular disease, the aHR for the primary outcome was 1.11 (0.99–1.24) in olmesartan users. The aHR for the primary outcome was increased in olmesartan users with CKD (aHR, 1.21 [1.04–1.41]).

Sensitivity Analysis Censoring Rather Than Excluding ARB Switchers

In this analysis (n=48 475), the aHRs comparing olmesartan with all other ARBs for the primary outcome were 1.02 (95% confidence interval, 0.97–1.08) in the overall cohort,

Table 1. Baseline Characteristics of Olmesartan and Other ARB Users

	Olmesartan Users (n=10 370)	Other ARB Users (n=34 815)	*P* Value
Age, y	53.7±9.3	54.4±9.7	<0.0001
Sex			0.3709
Men	5472 (53)	18 197 (52)	
Women	4898 (47)	16 618 (48)	
Annual income, US dollars	48 034±6052	48 380±6237	<0.0001
Type of insurance			<0.0001
Point of service	6003 (58)	19 722 (57)	
Exclusive provider	1901 (18)	5956 (17)	
Preferred provider	889 (9)	3399 (10)	
Health maintenance	1463 (14)	5267 (15)	
Independent	108 (1)	455 (1)	
Other	6 (0)	16 (0)	
Clinical parameters at baseline			
Adjusted Diagnostic Groups Comorbidity Score	11±9	13±10	<0.0001
History of CV disease			
Ischemic heart disease	1425 (14)	6400 (18)	<0.0001
Heart failure	333 (3)	2065 (6)	<0.0001
Myocardial infarction	89 (1)	645 (2)	<0.0001
Dyslipidemia	6270 (60)	20 823 (60)	0.2339
Hypertension	9067 (87)	38 745 (83)	<0.0001
Arrhythmia	535 (5)	2463 (7)	<0.0001
Valvular heart disease	400 (4)	1698 (5)	<0.0001
eGFR categories, mL/min			<0.0001
<30	50 (0.5)	388 (1)	
30 to <60	824 (8)	3313 (10)	
60 to <90	5768 (56)	18 564 (53)	
≥90	3728 (36)	12 500 (36)	
Albuminuria (≥5 g/dL)	612 (6)	2533 (7)	<0.0001
Total cholesterol, mg/dL	192±46	190±46	0.0023
Triglycerides, mg/dL	181±174	180±195	0.7589
HDL, mg/dL	47±13	48±14	0.1175
LDL, mg/dL	112±37	109±37	0.0008
A1c, %	7.1±1.7	7.3±1.8	<0.0001
Hemoglobin, g/dL	14.1±1.6	13.9±1.6	<0.0001
Medication use			
Metformin	3404 (32)	11 988 (34)	0.0024
Sulfonylureas	1956 (19)	7525 (22)	<0.0001
Thiazolidinediones	1579 (15)	5951 (17)	<0.0001
Insulin	1032 (10)	4511 (13)	<0.0001
RAS blocker (ACE inhibitor or direct renin inhibitor)	4148 (40)	13 509 (39)	0.0282
Statins	4026 (39)	13 689 (39)	0.3641
β-Blockers	2610 (25)	9384 (27)	0.0003
Dihydropyridine CCB	1805 (17)	5494 (16)	<0.0001
Non-dihydropyridine CCB	602 (6)	2119 (6)	0.2906
Nitrates	336 (3)	1545 (4)	<0.0001

(Continued)

Table 1. Continued

	Olmesartan Users (n=10 370)	Other ARB Users (n=34 815)	*P* Value
Diuretics	2641 (25)	8574 (24)	0.0820
Anticoagulants	227 (2)	1073 (3)	<0.0001
Antiplatelets	459 (4)	2157 (6)	<0.0001
Healthcare utilization			
Inpatient hospitalization in year before index?			<0.0001
0	9473 (91)	30 438 (87)	
1	744 (7)	3404 (10)	
≥2	153 (1)	973 (3)	
Frailty	429 (4)	1536 (4)	0.2282
Chronic conditions in year before index date			<0.0001
≤1	1900 (18)	6373 (18)	
2–5	6653 (64)	20 540 (59)	
≥5	1817 (18)	7902 (22)	
Medication possession ratio for DM-related medications	0.44±0.7	0.47±1.0	0.0005

Data are n (%) or mean±SD. A1c indicates hemoglobin A1c; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CV, cardiovascular; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; and RAS, renin angiotensin system.

1.07 (0.93–1.24) in pre-existing cardiovascular disease, and 0.91 (0.82–1.01) in CKD.

Dose–Response Sensitivity Analyses

Results of the dose–response analysis are summarized in Table S1 in the online-only Data Supplement. In the overall cohort and in the cardiovascular disease subgroup, higher doses of olmesartan were associated with significantly increased risk for the primary outcome. The dose–response analyses for valsartan showed similar results to olmesartan. However, the dose–response analysis for losartan did not show increasing risk with higher doses (Table S1).

Results of the analysis comparing individual ARB agents are summarized in Table S2. In this sensitivity analysis, olmesartan was not consistently associated with the highest risk of harm. Few statistically significant differences were found between agents. Exceptions were that losartan was associated with a borderline statistically significant increase in the primary end point in subjects with cardiovascular disease, and the other ARBs (candesartan, eprosartan, and irbesartan) were associated with a lower risk for the primary end point in the CKD subgroup only (Table S2). In both cases, this result was driven by significant reductions in hospitalizations but not mortality (data not shown).

Discussion

In this analysis of a clinically rich data set encompassing >45 000 patients with diabetes mellitus, after extensive multivariable adjustment, we found that olmesartan use compared with other ARB use was not associated with an increased risk of hospitalization or all-cause mortality in the overall cohort. In fact, there was a trend toward a lower relative hazard for cardiovascular hospitalizations. However, in the higher-risk subjects (those with pre-existing cardiovascular disease or CKD), the aHRs for this primary end point were increased, and this risk increase was statistically significant in subjects with CKD (however, this finding was not robust to sensitivity analysis). The increased risk was primarily driven by an increase in the relative hazard of all-cause hospitalization. When we examined cause-specific hospitalization, we found no statistically significantly increased risk for cardiovascular disease–related and gastrointestinal disease–related hospitalization. A dose–response analysis of olmesartan found an increased risk for the primary end point in the overall cohort and in subjects with cardiovascular disease. However, similar findings were observed in a dose–response analysis for valsartan (but not losartan). This suggests that higher doses might have been a marker of increased risk rather than a causative factor. Finally, in the agent-specific analysis, olmesartan was not consistently associated with the highest risk, and few statistically significant differences between agents were found. In aggregate, our results do not demonstrate a robust signal for harm with olmesartan use in patients with diabetes mellitus, with the possible exception of diabetes mellitus with CKD.

One prior, large retrospective cohort analysis comparing olmesartan with other ARBs has been published.[20] This study of 118 700 subjects enrolled in a single US national healthcare plan reported that olmesartan use was associated with a lower risk of cardiac events compared with valsartan,

Table 2. Outcome Comparisons in Olmesartan Users vs Users of All Other Angiotensin Receptor Blockers

Outcome	Time at Risk (Person-Years)	Events , n (%)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	*P* Value
All-cause hospitalization or mortality	16 040	1686 (16)	0.87 (0.83–0.92)	0.99 (0.94–1.05)	0.89
All-cause mortality	18 310	35 (0.3)	0.67 (0.47–0.97)	0.90 (0.62–1.30)	0.56
All-cause hospitalization	16 040	1678 (16)	0.87 (0.83–0.92)	0.99 (0.94–1.05)	0.91
CV disease–related hospitalization	17 951	311 (3)	0.67 (0.59–0.75)	0.88 (0.78–1.00)	0.051
GI disease–related hospitalization	17 647	498 (5)	0.98 (0.88–1.08)	1.09 (0.98–1.20)	0.10
Noninfective enteritis and colitis-related admissions	18 247	46 (0.4)	1.05 (0.75–1.47)	1.21 (0.87–1.69)	0.26

Models adjusted for age, sex, socioeconomic status, cardiovascular comorbidities, clinical laboratory data, prescription drugs, Adjusted Clinical Groups score, total number of hospital admissions in the year before the index data, total number of chronic conditions at baseline, frailty, and the time-varying propensity to receive olmesartan. CI indicates confidence interval; CV, cardiovascular; GI, gastrointestinal; and HR, hazard regression.

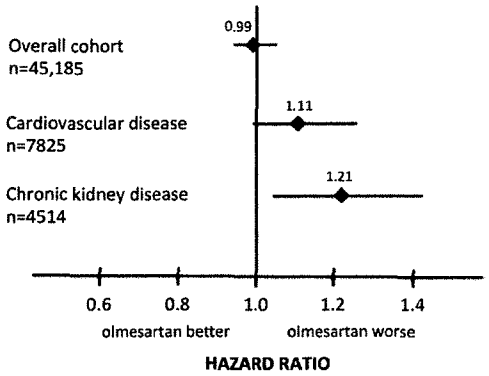

Figure 2. Adjusted hazard ratios and 95% confidence intervals for all-cause hospital admission or all-cause death according to olmesartan exposure.

irbesartan, and losartan. A limitation of this analysis was that olmesartan was prescribed to lower risk individuals, and no propensity score adjustment was used. In addition, the study population was broad and not limited to subjects with type 2 diabetes mellitus and no high-risk subgroup analyses were performed. Thus, although these findings are broadly consistent with the results of our study, they are not directly comparable because of differences in study populations and methodologic approaches.

Olmesartan is a third-generation high-affinity ARB with a 12- to 15-hour half-life that is prescribed once daily.[1,21] It is available as a dual combination product with hydrochlorothiazide or amlodipine and as a triple combination preparation with both of these agents.[21] No clinical trials demonstrating reductions in cardiovascular morbidity and mortality outcomes have been published.[22] The ongoing 1147 patient Supplemental Benefit of an Angiotensin Receptor Blocker in Hypertensive Patients with Stable Heart Failure Using Olmesartan (SUPPORT) trial is evaluating the efficacy of olmesartan compared with non-ARB antihypertensives in reducing a composite of all-cause mortality, nonfatal acute myocardial infarction, nonfatal stroke, and hospital admissions for heart failure.[23] Results are expected in 2013 to 2014.

Potential mechanisms to explain the association between olmesartan use and increased hospitalizations are not known. A J-curve mechanism resulting from excessive diastolic blood pressure lowering has been proposed to explain increased cardiovascular risk with olmesartan use in placebo-controlled studies.[3,4] Notably, previous studies comparing olmesartan with either placebo or atenolol therapy have reported that olmesartan leads to comparatively favorable improvements in such surrogate cardiovascular end points as vascular remodeling, endothelial dysfunction, inflammatory biomarkers, and atherosclerotic plaque volume.[24–26] In addition, olmesartan has been proposed to possess potential cardiovascular benefits compared with other ARBs because it is an inverse agonist at the angiotensin II type 1 receptor and because it reduces plasma angiotensin II levels.[23,27] Thus, overall, published data support the hypothesis that olmesartan should reduce rather than increase cardiovascular events. It is possible that mechanistic studies to assess potential harm have yet to be performed given that signals for potential harm have only been recently reported.

Similarly, no mechanisms to definitively explain the putative association between olmesartan and sprue-like enteropathy are known. Case reports indicate that symptoms appear months to years after olmesartan initiation.[28,29] Intestinal biopsies have revealed villous atrophy with mucosal inflammation and symptoms improve after drug discontinuation but not a gluten-free diet.[28,29] IgA transglutaminase antibodies are notably absent.[29] A cell-mediated or delayed hypersensitivity reaction, potentially associated with the human leukocyte antigen-DQ cell surface receptor type 2, has been proposed.[29]

Strengths of this study include the availability of a nationally representative, clinically rich data set; a relatively large sample size and long follow-up duration; a comparative effectiveness design in which olmesartan was compared directly against other ARBs; the use of advanced statistical techniques to adjust for potential confounders (including propensity score analysis); and conduction of extensive sensitivity analyses. Limitations include the retrospective, observational nature of the study design, the relatively short follow-up period (median 2.3 years was shorter than ROADMAP [median 3.2] and ORIENT [mean 3.2]), and the inability to adjust for additional potential confounders. The most important missing confounder was blood pressure, and we acknowledge that the observed differences in outcomes could have resulted from differences in blood pressure control. For example, in the overall cohort, subjects with losartan notably had less comorbidity at baseline, and the inability to adjust

Table 3. Subgroup Analyses in High-Risk Subjects Comparing Olmesartan Users With Users of All Other Angiotensin Receptor Blockers

	History of Cardiovascular Disease (n=8755)				CKD (GFR<60 mL/min; n=4575)			
Outcome	Adjusted HR (95% CI)	*P* Value	Time at Risk (Person -Years)	Events, n (%)	Adjusted HR (95% CI)	*P* Value	Time at Risk (Person-Years)	Events, n (%)
All-cause hospitalization or mortality	1.11 (0.99–1.24)	0.08	2008	363 (4)	1.21 (1.04–1.41)	0.02	1131	208 (5)
All-cause mortality	1.09 (0.59–2.03)	0.78	2462	12 (0)	0.88 (0.40–1.97)	0.76	1364	7 (0)
All-cause hospitalization	1.12 (0.99–1.25)	0.06	2008	362 (4)	1.23 (1.05–1.43)	0.009	1131	208 (5)
CV disease–related hospitalization	1.19 (0.98–1.46)	0.09	2335	115 (1)	1.30 (0.96–1.76)	0.09	1322	52 (1)
GI disease–related hospitalization	1.10 (0.87–1.37)	0.46	2348	91 (1)	1.27 (0.94–1.70)	0.12	1303	58 (1)
Noninfective enteritis and colitis-related admissions	1.13 (0.69–1.85)	0.62	2451	7 (0)	1.38 (0.79–2.42)	0.26	1351	9 (0)

CI indicates confidence interval; CV, cardiovascular; CKD, chronic kidney disease; GI, gastrointestinal; GFR, glomerular filtration rate; and HR, hazard regression.

for residual confounding may explain why there was a trend toward a lower hazard for the primary end point in olmesartan users in the overall group, yet risk was increased in the high-risk subgroups. Thus, it is important to emphasize that this type of study design provides associative and not causal evidence. In addition, all included subjects were middle aged Americans with commercial health insurance, which should be borne in mind when generalizing the results beyond this population. In particular, despite having cardiovascular risk factors or pre-existing disease, our study population had a crude death rate of only 392 per 100 000, which is lower than the 2010 crude death rate for all US adults aged 50 to 54 years (491.7 per 100 000)[30] and indicates that the study population was relatively healthy and well treated. Finally, we did not have information on cause-specific mortality and could not directly evaluate the association between olmesartan use and cardiovascular mortality.

Perspectives

Olmesartan is a commonly prescribed antihypertensive drug, and recent evidence linking this agent to an increased risk of cardiovascular mortality and sprue-like enteropathy mandates the need for further study. Analyses of large-scale clinical registry data serve as a useful and important complement to randomized controlled trial data in terms of assessing drug-related harm. In the present analysis, although there was a suggestion that patients with CKD may be at higher risk of all-cause mortality or hospitalization, findings that would be consistent with the results of the ROADMAP study,[3,4] our findings are not sufficiently robust or consistent to support the conclusion that olmesartan increases risk in patients with diabetes mellitus. About the subgroup of patients with CKD, given the results of ROADMAP and ORIENT and given our findings, we recommend that olmesartan use be used with caution in this patient population until further mechanistic, epidemiological, and interventional studies to clarify the effect of this drug on clinically important end points have been performed. We also recommend that further postmarketing surveillance of this agent be performed to assess risk in a more comprehensive fashion in different study samples and populations. This should take the form of additional analyses of clinical registries as well as a meta-analysis of individual patient-level data from previously published and soon-to-be-published randomized controlled trials.

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R. Padwal originated the study idea and all authors contributed to the conception and design, the analysis, and interpretation of data. D.T. Eurich and M. Lin had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. R. Padwal and D.T. Eurich wrote the initial manuscript draft, all authors revised it critically for important intellectual content, and all authors provided final approval of the version to be published. We would also like to acknowledge Betsey Jackson at Health Data Services Corporation (www.hdscorp.biz), PO Box 53, Carlisle, MA 01741 for providing independent database acquisition services.

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Novelty and Significance

What Is New?

- Olmesartan has been linked to an increased risk of cardiovascular mortality in patients with diabetes mellitus.
- We conducted a retrospective analysis of >45 000 subjects using a nationwide US-integrated insurance and laboratory claims database.
- In a risk-adjusted analysis that included propensity scores, no increased risk of all-cause mortality or hospitalization was found in our overall cohort although risk may be increased in patients with chronic kidney disease.

What Is Relevant?

- Olmesartan is commonly prescribed.
- To our knowledge, this is the first large comparative effectiveness study involving olmesartan in patients with diabetes mellitus.

Summary

We found no robust signal for harm and no compelling reason to avoid the drug except, perhaps, in patients with chronic kidney disease. Further study is required, especially in diabetics with chronic kidney disease.

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Comparative Effectiveness of Olmesartan and Other Angiotensin Receptor Blockers in Diabetes: Retrospective Cohort Study

Online Supplement

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Supplementary Methods

Dose-Response Sensitivity Analysis

A dose-response sensitivity analysis was also performed in which we used a standard (i.e., non-time dependent) Cox model to examine the association between tertiles of the average daily dose prescribed (low/medium/high) and the primary outcome in olmesartan users only. Subjects with the lowest level of exposure served as the reference group. Model covariates were identical to those used in the primary analysis except the propensity score adjusted for the propensity to receive a medium or high dose of olmesartan (compared to a low dose). To account for changes in dose over time, average daily dose was calculated by dividing the total dose prescribed over the follow-up period by the total drug exposure time. To calculate follow-up time, each subject was considered exposed to the drug until an event occurred (death or hospitalization), their insurance coverage was terminated or they discontinued therapy. If insurance coverage was terminated or treatment was discontinued, subjects were censored, with a censoring date of 60 days after the date on which their last prescription had ended. We also performed the same dose-response analysis for losartan and valsartan as a further sensitivity analysis. We did this to determine whether or not findings of the olmesartan dose-response analysis were similar for another ARB or specific to olmesartan alone.

Individual ARB Analysis

As a further sensitivity analysis, we performed an individual ARB analysis by dividing the primary cohort into separate ARB groups [olmesartan, losartan, valsartan, telmisartan and all others (candesartan, eprosartan and irbesartan)] and repeated the primary endpoint analysis (models adjusted as described above) to determine if olmesartan was associated with the highest risk of all-cause hospital admission or death. Olmesartan was used as the base comparator in this analysis, which was performed in the overall cohort and in the subgroups with pre-existing cardiovascular disease and chronic kidney disease. Subjects switching ARB agents were censored at the time the switch occurred.

Table S1. Sensitivity analysis examining the dose-response relationship within users of olmesartan, losartan and valsartan.

Group	Dose Tertiles	Medium Dose vs. Low Dose aHR (95% CI)	High Dose vs. Low Dose aHR (95% CI)
Olmesartan (n=10370)			
Overall cohort	Low: <18.7 mg Medium: 18.7-29.8 mg High: ≥29.9 mg	1.18 (1.04-1.34)	1.20 (1.05-1.37)
Cardiovascular disease	Low: <18.6 mg Medium: 18.6-30.1 mg High: ≥30.2 mg	1.62 (1.21-2.17)	1.40 (1.03-1.90)
Chronic kidney disease	Low: <19.9 mg Medium: 19.9-32.3 mg High: ≥32.4 mg	0.77 (0.51-1.14)	1.44 (0.99-2.10)
Losartan Sensitivity Analysis (n=8656)			
Overall cohort	Low: <37.4 mg Medium: 37.4-60.8 mg High: ≥60.8 mg	1.06 (0.96-1.19)	0.86 (0.77-0.97)

Cardiovascular disease	Low: <35.1 mg Medium: 35.1-56.2 mg High: ≥56.3 mg	1.14 (0.95-1.36)	0.86 (0.71-1.04)
Chronic kidney disease	Low: <36.6 mg Medium: 36.7-60.7 mg High: ≥60.8 mg	1.25 (0.96-1.63)	1.10 (0.83-1.47)
Valsartan Sensitivity Analysis (n=16004)			
Overall cohort	Low: <79.7 mg Medium: 79.8-143.1 mg High: ≥143.1 mg	1.24 (1.12-1.37)	1.43 (1.30-1.58)
Cardiovascular disease	Low: <78.33 mg Medium: 78.34-139.94 mg High: ≥140.0 mg	1.58 (1.32-1.89)	1.63 (1.36-1.94)
Chronic kidney disease	Low: <80.55 mg Medium: 80.57-147.42 mg High: ≥147.51 mg	0.71 (0.55-0.91)	1.06 (0.84-1.33)

aHR=adjusted hazard ratio; CI=confidence interval

Table S2. Sensitivity analysis comparing all-cause hospitalization or mortality in olmesartan users versus different ARBs

Agent (compared to olmesartan)	Overall Cohort (n=45185) HR (95% CI)	Cardiovascular Disease Subgroup (n=8755) HR (95% CI)	Chronic Kidney Disease Subgroup (n=4575) HR (95% CI)
Losartan (n=8656)	1.01 (0.94-1.08)	1.22 (1.07-1.40)	1.08 (0.90-1.30)
Valsartan (n=16004)	1.02 (0.96-1.09)	1.13 (0.99-1.28)	1.02 (0.86-1.20)
Telmesartan (n=3656)	0.94 (0.85-1.03)	1.09 (0.90-1.31)	0.87 (0.66-1.14)
All other ARBs (eprosartan, irbesartan, candesartan; n=6499)	1.00 (0.93-1.08)	1.03 (0.89-1.19)	0.79 (0.64-0.98)

Hazard ratios (HR) are relative to olmesartan (n=10370).

Exhibit J

Annual Adverse Drug Experience Report: 1996

October 30, 1997

Surveillance and Data Processing Branch
Division of Pharmacovigilance and Epidemiology
Office of Epidemiology and Biostatistics
Center for Drug Evaluation and Research
Food and Drug Administration

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INTRODUCTION

This report presents a descriptive overview of the 159,504 evaluable[1], postmarket adverse drug experience (ADE) cases received by the US Food and Drug Administration (FDA) during calendar year 1996[2]. A case consists of the original report of an ADE on a patient plus any follow-up information.

At this time, October, 1997, the SRS has accumulated about 1.4 million cases. The primary purpose for maintaining the database is to serve as an early warning or signaling system for ADEs not detected during premarket testing. The ADE system depends upon

detection of an adverse clinical event by a health professional or consumer, attribution of the clinical event to prior administration of a particular drug ("suspect" drug), and reporting of the ADE to the manufacturer of the suspected drug or directly to FDA. Data from these ADE cases are coded and entered into the computerized ADE database. Copies of the ADE cases are stored on microfilm or an imaging system. Up to five drugs per case may be entered into the computerized ADE database; the five can be a combination of "suspect" and "concomitant" drugs. Up to four adverse events per case and their associated body systems can by coded into the database, using FDA's "Coding Symbols for Thesaurus of Adverse Reaction Terms" (COSTART).

Reporting of postmarket ADEs by health professionals and consumers is voluntary. They may send their reports directly to FDA ("Direct" reports), to the drug manufacturer ("Manufacturer" reports), or both. Drug manufacturers are required by law and regulation to submit to FDA postmarket ADE reports received by any means from health professional or consumers.

It is important to remember certain caveats when using data from FDA's postmarket ADE database:

1. For any given ADE case, there is no certainty that the suspected drug caused the ADE. This is because physicians and consumers are encouraged to report all suspected ADEs, not just those that are already known to be caused by the drug. The adverse event may have been related to an underlying disease for which the drug was given, to other concomitant drugs, or may have occurred by chance at the same time the suspect drug was administered.
2. Accumulated ADE cases may not be used to calculate incidences or estimates of drug risk. Numbers from these data should be carefully interpreted as reporting rates and not occurrence or incidence rates.

Over the next pages, various kinds of data and information are presented on the postmarket ADE cases computerized into the FDA ADE database during calendar year 1996. Due to rounding, the percentages in tables and graphs may not total to 100%. Figures 1 and 2 present copies of the postmarket ADE forms used by manufacturers and health professionals or consumers, respectively.

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[1] Excludes "React Uneval" unevaluable reactions cases.

[2] The 1996 postmarket ADE Computerized data file used for this report was created October 1997.

Standard MedWatch Form, front page

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For use by user-facilities, distributors and manufacturers for MANDATORY reporting

Page ____ of ____

PLEASE TYPE OR USE BLACK INK

A. Patient information

1. Patient identifier — In confidence
2. Age at time of event: ____ or Date of birth:
3. Sex: ☐ female ☐ male
4. Weight: ____ lbs or ____ kgs

B. Adverse event or product problem

1. ☐ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
   - ☐ death ____
   - ☐ life-threatening
   - ☐ hospitalization – initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other: ____
3. Date of event
4. Date of this report
5. Describe event or problem
6. Relevant tests/laboratory data, including dates
7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1. Name (give labeled strength & manufacturer, if known)
   #1
   #2
2. Dose, frequency & route used
   #1
   #2
3. Therapy dates (if unknown, give duration)
   #1
   #2
4. Diagnosis for use (indication)
   #1
   #2
5. Event abated after use stopped or dose reduced
   #1 ☐ yes ☐ no ☐ doesn't apply
   #2 ☐ yes ☐ no ☐ doesn't apply
6. Lot # (if known)
   #1
   #2
7. Exp. date (if known)
   #1
   #2
8. Event reappeared after reintroduction
   #1 ☐ yes ☐ no ☐ doesn't apply
   #2 ☐ yes ☐ no ☐ doesn't apply
9. NDC # – for product problems only (if known)
   -
10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address
4. Operator of device
   - ☐ health professional
   - ☐ lay user/patient
   - ☐ other: ____
5. Expiration date
6. model # ____
   catalog # ____
   serial # ____
   lot # ____
   other # ____
7. If implanted, give date
8. If explanted, give date
9. Device available for evaluation? (Do not send to FDA)
   ☐ yes ☐ no ☐ returned to manufacturer on ____
10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Initial reporter

1. Name, address & phone #
   phone #
2. Health professional? ☐ yes ☐ no
3. Occupation
4. Initial reporter also sent report to FDA ☐ yes ☐ no ☐ unk

FDA

FDA Form 3500A (1/06)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

Standard MedWatch Form, back page

Medication and Device Experience Report
(continued)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

Refer to guidelines for specific instructions

Page ___ of ___

F. For use by user facility/distributor--devices only

1. Check one: ☐ user facility ☐ distributor
2. UF/Dist report number
3. User facility or distributor name/address
4. Contact person
5. Phone Number
6. Date user facility or distributor became aware of event
7. Type of report: ☐ initial ☐ follow-up # ___
8. Date of this report
9. Approximate age of device
10. Event problem codes (refer to coding manual): patient code / device code
11. Report sent to FDA? ☐ yes ☐ no
12. Location where event occurred: ☐ hospital ☐ home ☐ nursing home ☐ outpatient treatment facility ☐ outpatient diagnostic facility ☐ ambulatory surgical facility ☐ other:
13. Report sent to manufacturer? ☐ yes ☐ no
14. Manufacturer name/address

G. All manufacturers

1. Contact office -- name/address (& mfrng site for devices)
2. Phone number
3. Report source (check all that apply): ☐ foreign ☐ study ☐ literature ☐ consumer ☐ health professional ☐ user facility ☐ company representative ☐ distributor ☐ other
4. Date received by manufacturer
5. (A) NDA # ___ IND # ___ PLA # ___ pre-1938 ☐ yes OTC product ☐ yes
6. If IND, protocol #
7. Type of report (check all that apply): ☐ 5-day ☐ 15-day ☐ 10-day ☐ periodic ☐ initial ☐ follow-up # ___
8. Adverse event term(s)
9. Mfr. report number

H. Device manufacturers only

1. Type of reportable event: ☐ death ☐ serious injury ☐ malfunction (see guidelines) ☐ other: ___
2. If follow-up, what type? ☐ correction ☐ additional information ☐ response to FDA request ☐ device evaluation
3. Device evaluated by mfr? ☐ not returned to mfr. ☐ yes ☐ evaluation summary attached ☐ no (attach page to explain why not) or provide code:
4. Device manufacture date
5. Labeled for single use? ☐ yes ☐ no
6. Evaluation codes (refer to coding manual): method / results / conclusions
7. If remedial action initiated, check type: ☐ recall ☐ repair ☐ replace ☐ relabeling ☐ notification ☐ inspection ☐ patient monitoring ☐ modification/ adjustment ☐ other
8. Usage of device: ☐ initial use of device ☐ reuse ☐ unknown
9. If action reported to FDA under 21 USC 360(i), list correction/removal reporting number:
10. ☐ Additional manufacturer narrative and/or 11. ☐ Corrected data

Please do NOT return this form to either of these addresses.

FDA Form 3500A - back

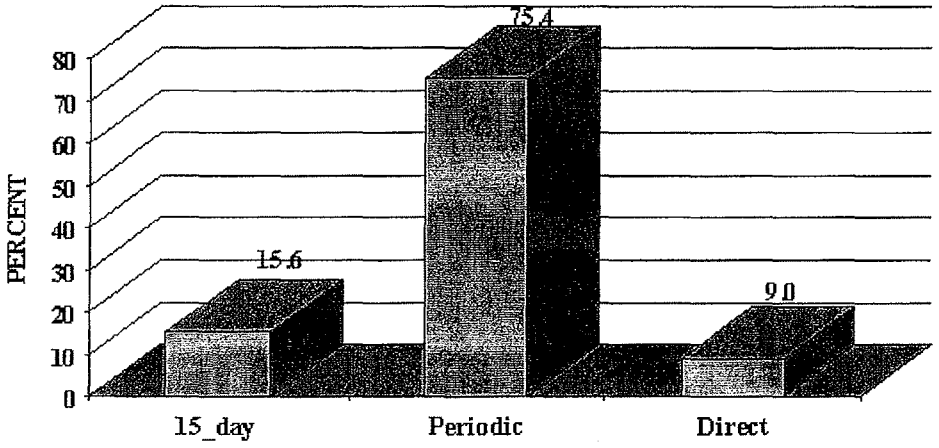
TYPES OF REPORTS

There are three types of reports in the FDA computerized postmarket ADE database:

1. Manufacturer-reported cases concerning ADEs not in present official FDA labeling with serious outcomes (i.e., death, life-threatening, hospitalization, permanent disability, congenital anomaly, cancer, or overdose). These cases are known in regulatory language as "**15-day Alert Reports**" because the manufacturer has 15 working days to submit this type of report to FDA.
2. All other manufacturer-reported cases. These cases are known in regulatory languages as "**Periodic Reports**" because the manufacturer is required to submit them to FDA on a cyclical basis.
3. Cases sent directly to FDA by health professionals or consumers ("**Direct Reports**").

As shown in Figure 3, reports submitted to FDA via manufacturers accounted for 91.0%(145,021) of the 159,504 postmarket ADE cases. Only 9.0%(14,483) were submitted directly to FDA. 15-day report were 15.6%(24,815) of the total.

Figure 3. Postmarket ADE Reports by Type of Report: 1996

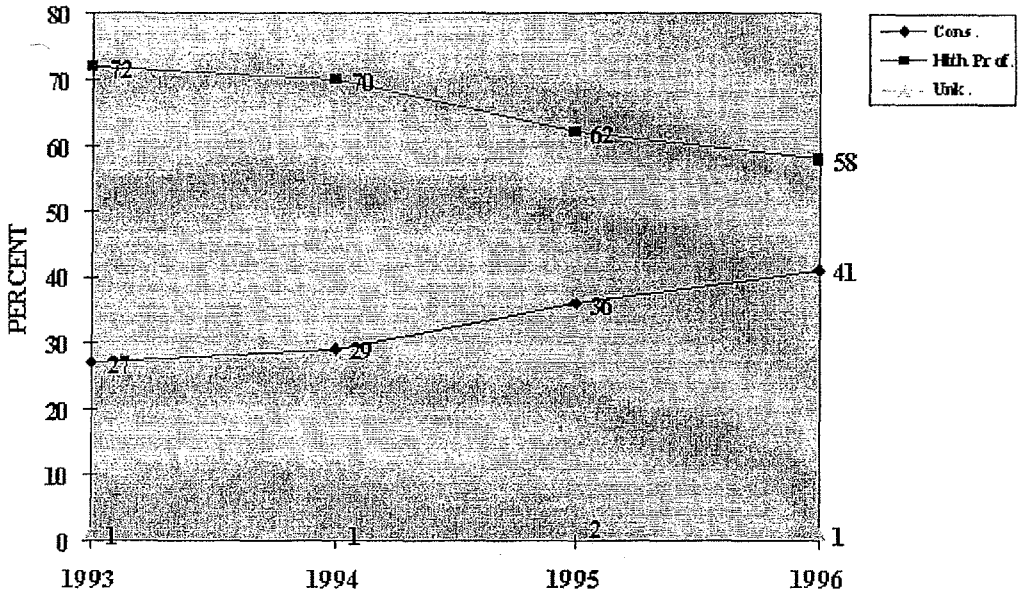


N = 159,504

REPORTING BY HEALTH PROFESSIONALS AND CONSUMERS

As shown in Figure 4, in 1996, there were 157,067 reporters for the 159,504 postmarket ADE cases, 64,752 (41.2%) reporters were consumers, 90,394 (57.6%) reporters were health professionals, and 1,921 (1.2%) were unknown sources. Figure 4 also shows that, over a four-year trend (1993-96), reports from consumers have increased both in absolute numbers and proportionally, whereas those from health professionals have gone up in absolute numbers.

Figure 4. ADE Reports By Health Professionals and Consumers, 1993-1996



Year: 1993 1994 1995 1996

N (000s)			N (000s)			N (000s)			N (000s)		
C	32		C	35		C	48		C	64	
H	86		H	84		H	81		H	90	
U	1		U	1		U	2		U	2	

GEOGRAPHIC LOCATION OF INITIAL REPORTER

As shown in Table 1, the initial reporter for 81.2% (129,521) of the 159,504 postmarket ADE cases was located within the US census regions; 9.6% (15,260) of cases were missing location.

There were 9.2% (14,723) of the postmarket ADE cases where the initial report source was foreign. There were four countries which each accounted for >= 9% of the foreign cases: France (31.2%), Japan (14.2%), United Kingdom (12.8%), Germany (9.2%).

Table 1. Postmarket ADE Reports by Geographic Location of Initial Reporter: 1996

	N	%
All Locations	***159,504***	***100***
US Census Region:	***129,521***	***81.2***
[a] New England	25,149	19.4
East South Central	23,355	18.0
Pacific	22,289	17.2
Middle West	22,207	17.2
West South Central	16,804	13.0
Middle Atlantic	16,763	12.9
Others	2,954	2.3
Foreign:	***14,723***	***9.2***
[b] France	4,593	31.2
Japan	2,094	14.2

United Kingdom	1,888	12.8
Germany	1,355	9.2
Others	4,793	32.6
Unknown	***15,260***	***9.6***

[a] US Census Regions are percentaged to 129,521
[b] Foreign countries are percentaged to 14,723

SEX AND AGE OF PATIENTS

As shown in Table 2, the ratio of female-to-male postmarket ADE cases was 1.7:1. For both females and males, the >= 60 year age group accounted for the greatest number of known sex-age cases.

Table 2. Postmarket ADE Reports by Reports by Sex & Age of Patient: 1996

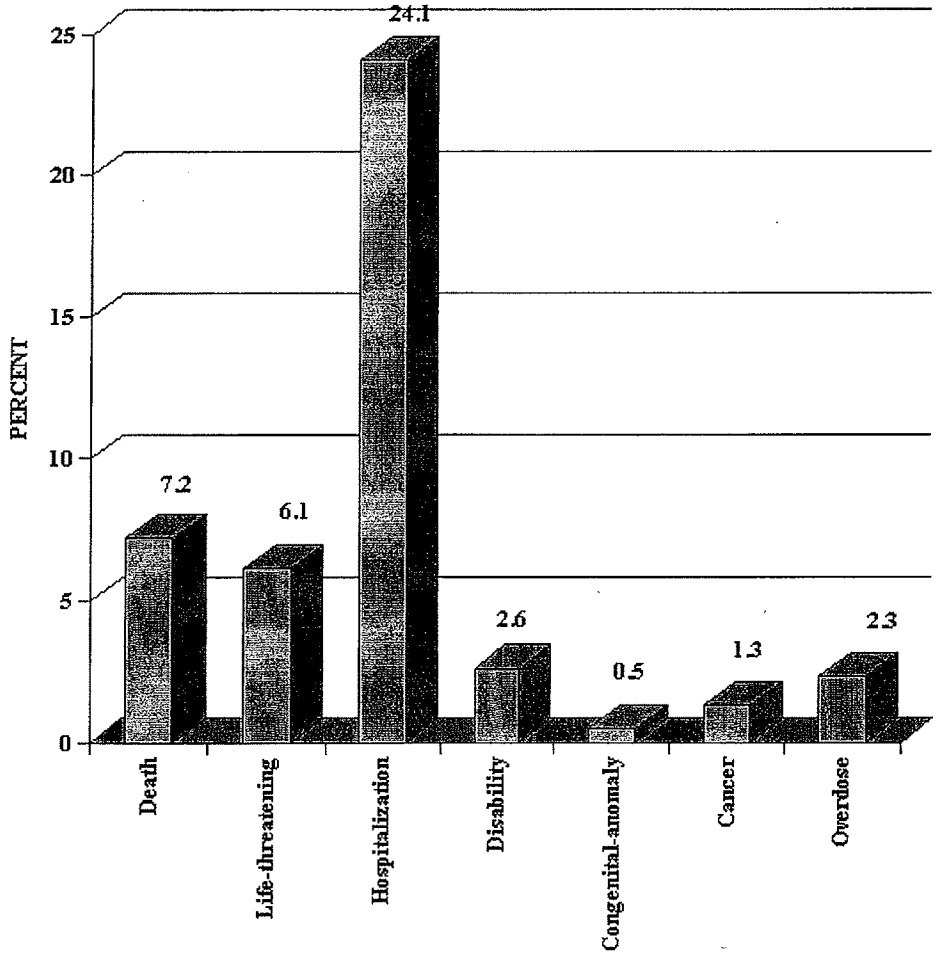
	N	%
ALL SEXES & AGES	***159,504***	***100***
All Females:	***91,200***	***57.2***
<= 19 yrs	5,971	3.7
20 - 39 yrs	19,855	12.4
40 - 59 yrs	20,980	13.2

>= 60 yrs	24,111	15.1
Unknown age	20,283	12.7
All Males:	***53,761***	***33.7***
<= 19 yrs	5,069	3.2
20 - 39 yrs	8,510	5.3
40 - 59 yrs	13,082	8.2
>= 60 yrs	17,418	10.9
Unknown age	9,682	6.1
Unknown Sex:	***14,543***	***9.1***
<= 19 yrs	439	0.3
20 - 39 yrs	163	0.1
40 - 59 yrs	242	0.2
>= 60 yrs	312	0.2
Unknown age	13,387	8.4

SERIOUS OUTCOMES

As shown in Figure 5, hospitalization was the most recorded serious outcome; congenital anomaly, the least. (One case could have more than one outcome).

Figure 5. Postmarket ADE Reports by Type of Serious Report: 1996



Serious Outcome

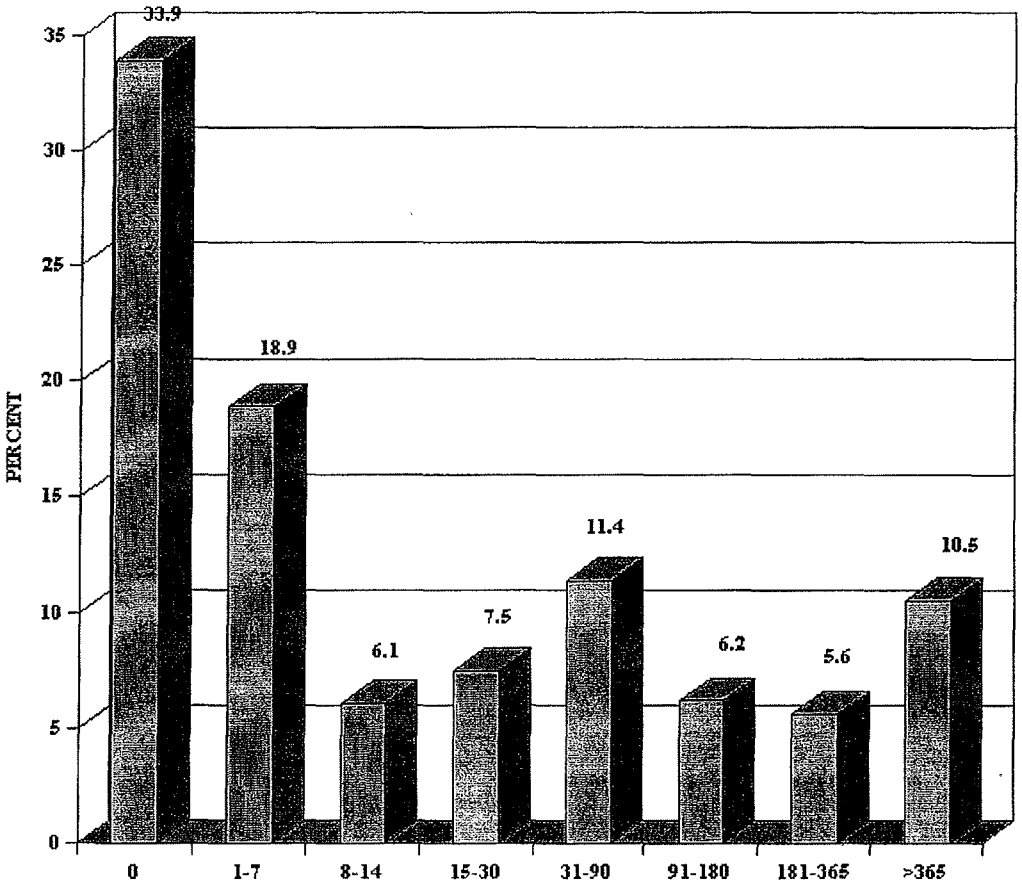
N = 105,599

LATENCY BETWEEN SUSPECT DRUG ADMINISTRATION AND ADE ONSET

As shown in Figure 6, of the 159,504 postmarket ADE cases, 53.6% (85,517) had both a drug start date and an adverse experience onset date for the first-listed suspect drug and first-listed adverse experience, respectively, and the drug date was computerized as

occurring before the adverse experience date. About half of these cases noted that the adverse event occurred within one week of drug initiation.

Figure 6. Postmarket ADE Reports by Latency Period: 1996



Latency (days)

N = 85,517

CLASSES OF SUSPECT DRUGS

Table 3 presents the top-10 ranked drug classes associated with the 174,905 suspect drugs computerized from the 159.504 postmarket ADE cases. The top-ranked drug class, central nervous system agents, accounted for approximately little less than one-quarter of

the drug class mentions[3]. Together with the second and third ranked drug classes, anti-infectives, and hormones and synthetic substitutes, these top three ranked drug classes comprised about half of the total drug class mentions.

Table 3. Postmarket ADE Reports by Top-10 Ranked Classes of Suspect Drugs: 1996

	N	%
All Suspect Drug Mentions	*174,905*	*100*
Central nervous system agents	39,541	22.6
Anti-infective agents	21,388	12.2
Hormones & synthetic substitutes	20,956	12.0
Cardiovascular drugs	18,076	10.3
Skin & mucous membrane agents	13,927	7.9
Antineoplastic agents	12,552	7.2
Gastrointestinal drugs	10,580	6.0
Unclassified therapeutic agents	10,397	5.9
Autonomic drugs	8,189	4.7
Blood formation and coagulation	3,707	2.1

[3] The drug classification used was the American Hospital Formulary Service Pharmacologic - Therapeutic Classification (American Society of Health-System Pharmacists, Bethesda, Maryland, 1997)

SUSPECT DRUGS BY ENTRY NAME AND NEW MOLECULAR ENTITY STATUS

Table 4 shows the top-10 ranked suspect drugs as entered on the 159,504 postmarket ADE reporting forms.

New Molecular Entities (NMEs) are defined as new drugs approved within the past three years. For this 1996 report, NMEs are new drugs approved during 1993-96. Of the 174,905 suspect drugs computerized from the 159,504 postmarket ADE cases, 30.2%(29,584) involved NMEs.

Table 4. Postmarket ADE Reports by Top-10 Ranked Suspect Drugs: 1996

	N	%
All Suspect Drug Mentions	***174,905***	***100***
Fosamax™	6,197	3.5
Norplant™	5,957	3.4
Prozac™	3,506	2.0
Pepcid AC™	3,104	1.8
Estraderm™	2,890	1.7
Femstat™	2,648	1.5
Rogaine™	2,435	1.4
Paragard™ T380A	2,172	1.2
Nix™	2,077	1.2
Zoloft™	2,070	1.2

™ - Trademark

DRUG CLASSES STRATIFIED BY HEALTH PROFESSIONALS OR CONSUMERS, TYPE OF REPORT, AND YEAR

Table 5 shows the top-five ranked drug classes[3] associated with suspect drugs, stratified by whether the initial reporter was a health professional or consumer, the type of report, and year the cases was computerized into the FDA postmarket ADE database.

1996 Data. In 1996, there were 155,529 drug class mentions where type of initial reporter and type of report were known. For consumers, only two of the top-five ranked drug classes were common to all report types: central nervous system agents and hormones and synthetic substitutes. For health professionals, there were four drug classes of the top-five ranked drug classes common to all report types: central nervous system agents, antineoplastic agents, anti-infective agents, and cardiovascular drugs. The only drug class in the top-five ranked drug classes common to both consumers and health professionals across report types was central nervous system agents.

Table 5. Top-5 Ranked Drug Classes Per Type of Reporter & Report: 1996

Reporter Type	Report Type	Drug Class	N	%
ALL	*ALL*	*ALL*	*155,529*	*100*
Consumer	*All*	*All*	*64,858*	*41.7*
	Mfr 15-day	*All*	*2,820*	*1.8*
		Central nervous system agents	689	0.4
		Hormones and synthetic substitutes	482	0.3
		Anti-infective agents	309	0.2
		Cardiovascular drugs	271	0.2
		Autonomic drugs	233	0.1

	Mfr Periodic	*All*	*61,225*	*39.4*
		Hormones and synthetic substitutes	11,709	7.5
		Skin and mucous membrane agents	10,612	6.8
		Central nervous system agents	10,073	6.5
		Gastrointestinal drugs	7,080	4.6
		Cardiovascular drugs	5,504	3.5
	Direct	*All*	*813*	*0.5*
		Central nervous system agents	222	0.1
		Skin and mucous membrane agents	132	0.1
		Autonomic drugs	88	0.1
		Anti-infective agents	87	0.1
		Cardiovascular drugs	43	0.0
Health Professional	*All*	*All*	*90,671*	*58.3*
	Mfr 15-day	*All*	*20,200*	*13.0*
		Central nervous system agents	4,264	2.7
		Anti-infective agents	3,851	2.5
		Antineoplastic agents	3,165	2.0
		Cardiovascular drugs	2,582	1.7
		Hormones and synthetic substitutes	1,274	0.8
	Mfr Periodic	*All*	*56,998*	*36.6*

		Central nervous system agents	15,324	9.9
		Anti-infective agents	8,061	5.2
		Cardiovascular drugs	5,953	3.8
		Hormones and synthetic substitutes	5,434	3.5
		Antineoplastic agents	3,962	2.5
	Direct	*All*	*13,473*	*8.7*
		Central nervous system agents	3,713	2.4
		Anti-infective agents	2,477	1.6
		Cardiovascular drugs	1,736	1.1
		Antieoplastic agents	1,398	0.9
		Blood formation and coagulation	919	0.6

ROUTES OF SUSPECT DRUGS

Table 6 presents the top-10 ranked routes of administration associated with the suspect drugs. There were 156,759 routes mentioned in conjunction with the 159,504 postmarket ADE cases. About three-fifths of the route mentions noted the oral route of administration.

Table 6. Postmarket ADE Reports by Top-10 Ranked Routes of Administration of Suspect Drugs: 1996

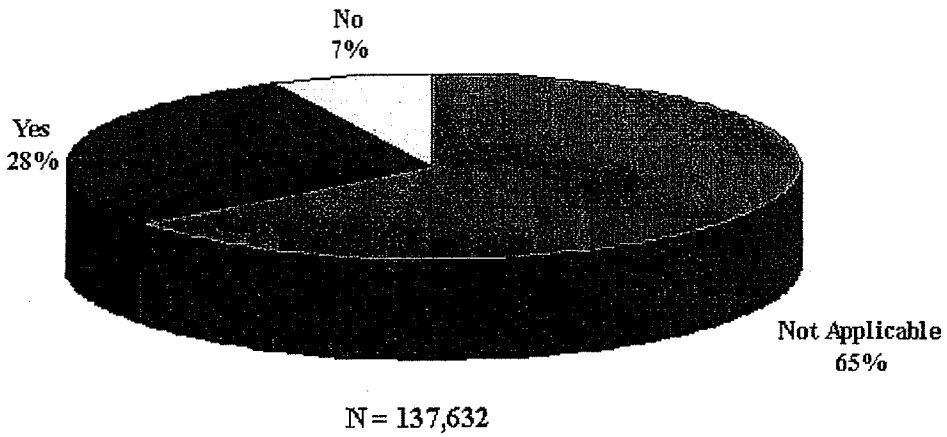
	N	%
All Routes	*156,759*	*100*

Oral	99,421	63.4
Intravenous	14,873	9.5
Subcutaneous	8,204	5.2
Topical	8,181	5.2
Transdermal	7,460	4.8
Vaginal	3,798	2.4
Inhalation	2,739	1.7
Intrauterine	2,318	1.5
Ophthalmic	2,094	1.3
Intramuscular	2,029	1.3

ABATEMENT OF ADVERSE EVENT

For the 174,905 suspect drug mentions, 78.7% (137,632) had an answer to the question of whether the adverse event abated after the suspect drug was stopped or the dose was reduced. Figure 7 shows the distribution of responses. About one-quarter of these 137,632 abate mentions indicated a positive dechallenge ("Yes" response).

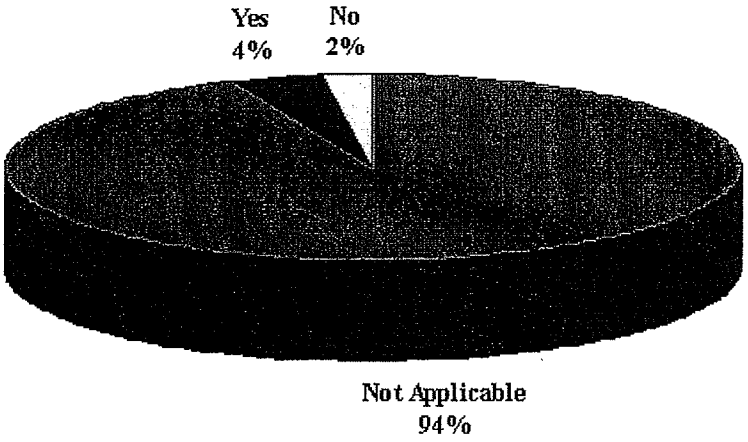
Figure 7. Postmarket ADE Reports by Abate response: 1996



REOCCURRENCE OF ADVERSE EVENT

For the 174,905 suspect drug mentions, 76.2% (132,296) had an answer to the question of whether the adverse event reappeared after reintroduction of the suspect drug. Figure 8 shows the distribution of responses. Four percent (5,309) of these 132,296 reoccur mentions indicated a positive rechallenge ("Yes" response).

Figure 8. Postmarket ADE Reports by Reintroduction Response: 1996

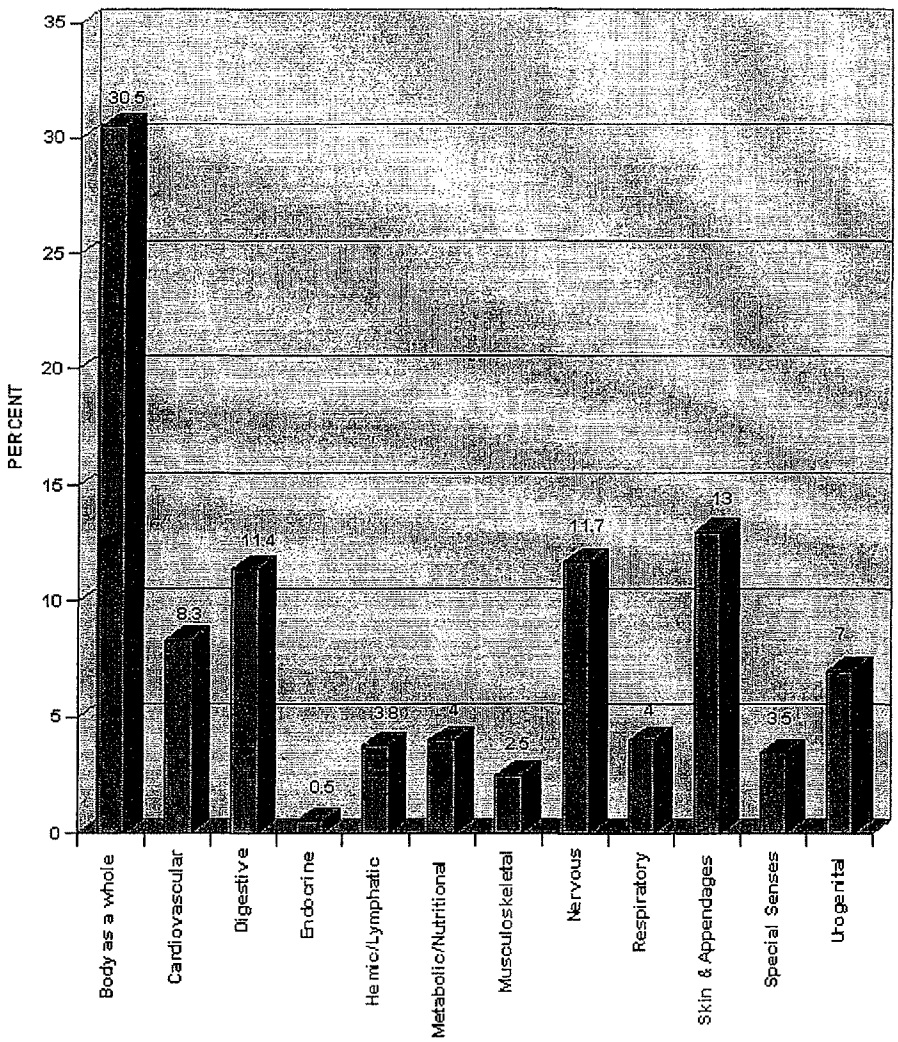


N = 132,296

BODY SYSTEMS

There were 159,515 body system mentions associated with the adverse events of the 159,504 postmarket ADE cases. The distribution of these mentions across the 12 body system mentions is presented in Figure 9. Four body systems each had > 10% of the 159,515 body system mentions: body as a whole (systemic adverse events) - 30.5%, skin and appendages system - 13%, nervous system - 11.7%, and digestive system - 11.4%.

Figure 9. Postmarket ADE Reports by Body System: 1996



N = 159,515

ADVERSE EVENTS

Table 7 shows the top-10 ranked adverse events reported with the 159,504 postmarket ADE cases. The top ranked ADE was " No drug effect: - 10% of the ADE cases reported this event.

Table 7. Top-10 Ranked Adverse Events: 1996

Adverse Event	N	%
All Postmarket ADE Reports	*159,504*	*100*
No drug effect	15,918	10.0
Headache	5,133	3.2
Rash	4,090	2.6
Application site reaction	3,583	2.2
Diarrhea	2,445	1.5
Urticaria	2,373	1.4
Alopecia	2,237	1.4
Aggravation of existing reaction	2,236	1.4
Dizziness	2,002	1.3
Abdominal pain	1,875	1.2

DRUG CLASSES ASSOCIATED WITH BODY SYSTEM ADVERSE EVENTS

Table 8 presents the four body systems comprising the most adverse events, each of which has been crosstabulated by its top-five ranked suspect associated drug classes[3]. Three drug classes were in the top-five ranks for all four body systems, central nervous system agents, cardiovascular drugs, and anti-infective agents.

Table 8. Top-4 Ranked Body Systems with Their Respective Top-5 Ranked Suspect Drug Classes: 1996

Body System	Suspect Drug Class	N	%
Body as a whole	***All***	***53,050***	***100***
	Central nervous system agents	12,131	22.9
	Hormones and synthetic substitutes	7,216	13.6
	Skin and mucous membrane agents	6,378	12.0
	Anti-infective agents	4,816	9.1
	Cardiovascular drugs	4,566	8.6
Skin and Appendages	***All***	***21,792***	***100***
	Hormones and synthetic substitutes	3,948	18.1
	Skin and mucous membrane agents	3,689	16.9
	Anti-infective agents	3,178	14.6
	Central nervous system agents	2,941	13.5
	Cardiovascular drugs	1,931	8.9
Nervous System	***All***	***20,515***	***100***
	Central nervous system agents	8,265	40.3
	Anti-infective agents	2,209	10.8
	Cardiovascular drugs	1,763	8.6
	Hormones and synthetic substitutes	1,463	7.1
	Autonomic drugs	1,425	7.0
Digestive System	***All***	***20,059***	***100***

	Central nervous system agents	4,105	20.5
	Anti-infective agents	4,081	20.3
	Gastrointestinal drugs	2,355	11.7
	Unclassified therapeutic agents	2,256	11.2
	Cardiovascular drugs	1,900	9.5

ANNUAL FOI REPORT

1996

In 1996, the Surveillance and Data Processing Branch (SDPB) received a total of 2,162 Freedom of Information (FOI) requests. These requests were for adverse reaction cases collected by the Food and Drug Administration's Spontaneous Reporting System (SRS). All requests are logged in by the central FOI office and triaged to various responsive divisions throughout the Center for Drugs.

SDPB processed FOI requests utilizing several forms of data accession. Compressed ASCII files were provided to mostly third-party businesses. Microfiche line listings or paper copies were also available depending on the preference of the requester. Case reports from the SRS database were obtained by people wanting a formalized version of the Medwatch form.

Law firms comprised the most FOI requests, with third-party organizations ranking second. Third were the pharmaceutical companies and last were consumers. However, consumers made more inquiries in 1996 than in previous years. This could have been attributed to media reporting and those consumers wanting to establish a more significant role in their drug therapy.

Hal Stepper

Exhibit K

2014 WL 12586426
Only the Westlaw citation is currently available.
United States District Court,
S.D. Ohio, Western Division.

Shirley Monroe, et al., Plaintiffs,
v.
Novartis Pharmaceuticals Corporation, Defendant.

Case No. 1:12-cv-746
|
Signed 09/15/2014

Attorneys and Law Firms

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ORDER GRANTING IN PART AND DENYING IN PART DEFENDANT'S MOTION TO EXCLUDE THE TESTIMONY OF DR. SUZANNE PARISIAN [1]

1 It is unclear whether Defendant's motion to exclude seeks to exclude all of Dr. Parisian's testimony, or only certain portions of her testimony. (Doc. 56). For purposes of this Order, the Court assumes Defendant seeks to exclude all of Dr. Parisian's testimony.

Timothy S. Black, United States District Judge

**1 This civil action is before the Court on Defendant's motion to exclude the testimony of Dr. Suzanne Parisian (Doc. 56), and the parties' responsive memoranda (Docs. 60, 66).

I. FACTUAL BACKGROUND

This case is one of hundreds of similar cases involved in nationwide litigation that has gone on for approximately ten years against Novartis Pharmaceuticals Corporation, the manufacturer, marketer, and distributor of the drugs Aredia® and Zometa®. (Doc. 64 at ¶ 5). Aredia® and Zometa® were approved by the Food and Drug Administration ("FDA") for treatment of bone cancer and other bone diseases and conditions. (*Id.* at ¶ 7). Plaintiffs allege that Novartis should have known that the drugs would have an increased effect on bones that remodel at a faster rate, such as the jaw bone. (*Id.* at ¶ 11). This process allegedly results in osteonecrosis of the jaw ("ONJ"), or death of the jaw bone. (*Id.* at ¶ 1). ONJ causes the patient to lose their jaw bone. (*Id.*)

On May 26, 2010, Plaintiffs Mr. and Mrs. Monroe brought suit against Novartis, alleging that Mrs. Shirley Monroe suffered ONJ caused by infusions of Zometa®>.[2] Plaintiffs assert five claims in the amended complaint. (*See* Doc. 64 at ¶¶ 24-60). Four claims are based on the Ohio Products Liability Act ("OPLA"), Ohio Revised Code § 2307.71, *et seq.*, for inadequate warning, nonconformance with manufacturer's representation, design defect, and punitive and exemplary damages. (*Id.* at ¶¶ 24-57). The fifth claim is a common law loss of consortium claim filed on behalf of Mr. William Monroe, Jr. (*Id.* at ¶¶ 58-60).

2 Mrs. Shirley Monroe died on February 26, 2012 and her claims passed to the executor of her estate on June 5, 2012. (*See* Doc. 95-1 at 2). Mr. William Monroe, Jr. died on June 6, 2014. (*Id.*) Today, by separate Order, the Court grants the motion to dismiss Mr. Monroe's loss of consortium claim. (*Id.*)

Novartis seeks to exclude the testimony of one of Plaintiffs' industry experts, Dr. Suzanne Parisian. (Doc. 56). Dr. Parisian is a board-certified pathologist and operates MD Assist, Inc., her own regulatory and medical consulting firm, which specializes in FDA regulation issues. (Doc. 94-1 at 123, 136). The purpose of Dr. Parisian's testimony is to address four issues:

(1) the role, process and functions of the FDA and the responsibilities of pharmaceutical drug sponsors;

(2) Novartis' conduct regarding New Drug Application ("NDA") approvals and post-approval of its two intravenous bisphosphonates, Aredia® and Zometa®;

(3) Novartis' pharmacovigilance efforts,[3] investigation of ONJ, and interactions with FDA; and

(4) Novartis' communication of ONJ risks to health care providers.

(Doc. 56-13 at 8).

3 Pharmacovigilance is post-market product surveillance. (*See* Doc. 56-13 at 33).

II. STANDARD OF REVIEW

Both parties cite an exhaustive list of cases where Dr. Parisian's testimony was accepted, excluded, or limited.[4] While these cases are persuasive, this Court is bound only by *Daubert*, Federal Rule of Evidence 702, the Sixth Circuit, the Supreme Court, and to some extent, the MDL. *See Deutsch v. Novartis Pharms. Corp.*, 768 F. Supp. 2d 420, 464 (E.D.N.Y. 2011).

4 Counsel aptly observes the importance of avoiding a "colossal waste of judicial and legal resources" (Doc. 60 at 7), yet this Court had to spend significant time and resources reviewing the issues that were raised in various other Novartis cases pending around the country, because the motions to exclude filed with this Court were boilerplate and lacked relevant details. Specifically, counsel failed to include relevant citations, pin points, and properly attached and cited exhibits. In fact, this Court did not even have Dr. Parisian's curriculum vitae to review until it expressly requested its production.

***2** Rule 702 of the Federal Rules of Evidence permits testimony based on "scientific, technical, or other specialized knowledge" by experts qualified by "knowledge, skill, experience, training, or education" if the testimony is both relevant and reliable. Fed. R. Evid. 702. The trial judge must act as a gatekeeper, only admitting expert testimony which is relevant and reliable. *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 589 (1993). As a gatekeeper, the trial judge has discretion in determining whether an expert's testimony is admissible based on whether the testimony is both relevant and reliable. *Johnson v. Manitowoc Boom Trucks, Inc.*, 484 F.3d 426, 429 (6th Cir. 2007). *Daubert* attempts to strike a balance between liberal admissibility for relevant evidence and the need to exclude misleading "junk science." *Best v. Lowe's Home Ctrs., Inc.*, 563 F.3d 171, 176-77 (6th Cir. 2009). An expert must utilize the "same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Id.* at 177.

The relevancy requirement stems from Rule 702's mandate that the testimony "assist the trier of fact to understand the evidence or to determine a fact in issue." *Best*, 563 F.3d at 591. Relevance means that "there must be a 'fit' between the inquiry in the case and the testimony." *United States v. Bonds*, 12 F.3d 540, 555 (6th Cir. 1993). The reliability requirement is drawn from Rule 702's requirement that the subject of an expert's testimony be "scientific knowledge." *Daubert*, 509 U.S. at 589-90. In this context, reliability means "evidentiary reliability" or "trustworthiness" which in turn connotes "scientific validity." *Bonds*, 12 F.3d at 555. A party proffering expert testimony has the burden of demonstrating by a "preponderance of proof that the expert whose testimony is being offered is qualified and will testify to scientific knowledge that will assist the trier of fact in understanding and disposing of issues relevant to the case." *Pride v. BIC Corp.*, 218 F.3d 566, 578 (6th Cir. 2000) (internal quotations omitted).

The trial court's objective "is to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999). The trial judge enjoys broad discretion in determining whether the *Daubert* factors reasonably measure reliability in a given case. *Id.* at 153. With this framework in mind, the Court will now address Defendant's motion.

III. ANALYSIS

A. Reliability

In the context of non-scientific expert testimony, the Court focuses on the witness's "personal knowledge and experience" in determining reliability:

> The Court [in *Khumo Tire*] stressed, however, that "*Daubert's* list of specific factors neither necessarily nor exclusively applies to all experts or in every case." In some cases (even cases involving non-scientific expert testimony), the factors may be pertinent, [*sic*] while in

> other cases "the relevant reliability concerns may focus upon personal knowledge or experience." "Whether *Daubert*'s specific factors are, or are not, reasonable measures of reliability in a particular case is [*sic*] a matter that the law grants the trial judge broad latitude to determine."

First Tennessee Bank Nat. Assoc. v. Barreto, 268 F.3d 319, 335 (6th Cir. 2001) (citations omitted). The Sixth Circuit has specifically held that the reliability of non-scientific expert testimony depends on the facts and circumstances of the case and can be established through the credentials of the expert. *Id.*

Defendant argues that Dr. Parisian is not qualified to testify in this case because she does not have any experience working for a pharmaceutical company and her work at the FDA was in the regulation of medical devices, not pharmaceuticals. (Doc. 56-1 at 5). However, it is clear from her curriculum vitae that Dr. Parisian has extensive personal and professional experience as a clinical pathologist and consultant on the FDA approval process for both medical devices and pharmaceuticals. (Doc. 94-1 at 123). Defendant can certainly question her qualifications on cross-examination.

***3** Accordingly, Plaintiffs have established that Dr. Parisian has the requisite credentials to give reliable testimony.

B. Relevance

Evidence is relevant if: (1) "it has any tendency to make a fact any more or less probable than it would be without the evidence;" and (2) if it "is of consequence in determining the action." Fed. R. Evid. 401.

1. Regulatory Compliance

Dr. Parisian's report refers to numerous alleged violations of FDA regulations and federal law. (*See* Doc. 56-13). Defendant seeks to exclude any testimony about its alleged violations of FDA regulations. (Doc. 56-1 at 9). Specifically, Plaintiffs' claims were brought under the OPLA; therefore, any discussion of FDA violations, the FDCA, or any other section of Title 21 of the Code of Federal Regulations, is irrelevant. [5] Plaintiffs cannot "have [their] cake and eat it too; [they] cannot bring common law claims not grounded in FDA regulations only to present an expert to opine on whether defendant violated those regulations." *Hogan v. Novartis Pharms. Corp.*, No. 06-civ-260, 2011 U.S. Dist. LEXIS 43800, at *5 (E.D.N.Y. Apr. 23, 2011) (excluding Dr. Parisian's testimony where the plaintiff had not brought separate federal claims). "[T]he Court will not permit defendant to litigate the case in the shadow of the FDA." *Id.*

5 The Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C.S. §§ 301, *et seq.*, does not imply or include any civil private rights of action. *Griffin v. O'Neal, Jones & Feldman, Inc.*, 604 F. Supp. 717, 720 (S.D. Ohio 1985).

Therefore, Dr. Parisian's testimony regarding alleged violations of the FDA or other federal regulations is irrelevant and excluded.

2. Regulatory Causation

Next, Defendant maintains that Dr. Parisian will testify about regulatory causation. Specifically, Dr. Parisian will testify about the types of evidence that the FDA would consider in determining the "association of a serious hazard with a drug." (Doc. 60 at 9). However, regulatory causation is not recognized as a legitimate form of causation. *See, e.g.*, *Matthews v. Novartis Pharms. Corp.*, No. 3:12-cv-314, 2013 U.S. Dist. LEXIS 153519, at *67-68 (S.D. Ohio Sept. 20, 2013) (finding the distinction between medical causation and regulatory causation to be misleading and confusing for the jury). In fact, Dr. Parisian does not even address regulatory causation in her report. [6]

6 Dr. Parisian's report appears to be a boilerplate report that was submitted in all of the Novartis cases. The report lacks any specific findings with respect to the facts of this case. (*See* Doc. 60). Accordingly, it is especially difficult for this Court to address the relevance of Dr. Parisian's opinions, when it is unclear what she will opine with respect to this case.

Accordingly, Dr. Parisian is precluded from testifying about regulatory causation.

3. Labeling and Adequacy of Warning

Dr. Parisian will also testify about the standard FDA regulations regarding product labeling in the pharmaceutical industry. (Doc. 60). Specifically, she will testify about how the FDA regulations apply to the labeling process and the adequacy of the warnings generally, in order to explain "the role, process and functions of the FDA and the responsibilities of pharmaceutical drug sponsors." (Doc. 56-13 at 8).

***4** The Court finds that Dr. Parisian is qualified to testify generally about the FDA labeling process and the adequacy of warnings. Although, direct evidence of FDA violations is not relevant, it may assist the trier of fact to understand the requirements for product labeling in the pharmaceutical industry and how companies meet the FDA's standards. This may include how the labels are written and communicated to health care providers. Dr. Parisian may also testify generally about what the FDA regulations require of drug manufacturers and how they communicate "risks to health care providers." (Doc. 56-13 at 8).

4. Other Irrelevant or Unfairly Prejudicial Testimony

Defendant argues that Dr. Parisian's testimony will also include irrelevant and unfairly prejudicial criticisms of the FDA and the pharmaceutical industry, opinions about drugs other than Aredia® and Zometa®, and injuries other than ONJ. (Doc. 56-1 at 16). Plaintiffs maintain that Dr. Parisian will not testify about these issues.[7] Dr. Parisian will not be permitted to offer irrelevant or unfairly prejudicial testimony.

7 Defendant also argues that Dr. Parisian will testify about the medical causation of ONJ, Defendant's corporate state of mind, industry standards, the monitoring of the safety of clinical trial patients during the FDA approval process, and the ghostwriting and funding of publications. (Doc. 56-1 at 9-12, 15-16). Plaintiffs maintain that Dr. Parisian will not testify about these issues. (Doc. 60 at 10).

Additionally, Defendant alleges that Dr. Parisian's testimony will be infused with legal conclusions. (Doc. 56-1 at 7-9). Legal conclusions are to be determined by the trier of fact. *See Matthews*, 2013 U.S. Dist. LEXIS 153519 at 65. Therefore, Dr. Parisian will not be permitted to make any legal conclusions.

IV. CONCLUSION

Accordingly, for the foregoing reasons, Defendant's motion to exclude Dr. Suzanne Parisian's testimony (Docs. 56) is **GRANTED IN PART** and **DENIED IN PART** as explained in this Order.

IT IS SO ORDERED.

Date: 9/15/14.

All Citations

Slip Copy, 2014 WL 12586426

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Exhibit L

LEXSEE

Positive
As of: Mar 29, 2017

ALVIN MATHEWS, Plaintiff, v. NOVARTIS PHARMACEUTICALS CORPORATION, Defendant.

Case No. 3:12-cv-314

UNITED STATES DISTRICT COURT FOR THE SOUTHERN DISTRICT OF OHIO, WESTERN DIVISION

2013 U.S. Dist. LEXIS 153519; CCH Prod. Liab. Rep. P19,255

September 20, 2013, Decided
September 25, 2013, Filed

PRIOR HISTORY: Mathews v. Novartis Pharms. Corp., 953 F. Supp. 2d 811, 2013 U.S. Dist. LEXIS 99495 (S.D. Ohio, July 12, 2013)

CORE TERMS: warning, dental, bisphosphonate, causation, patient, summary judgment, expert witness testimony, manufacturer, label, screening, jaw, pretreatment, clinical trials, bisphosphonate-induced, bone, invasive, dosing, admissible, incidence, reliable, admissibility, transferor, genuine, adequacy, exposed, dentist, inadmissible, therapy, warn, product liability

COUNSEL: [*1] MDL Clerk of Court, Interested Party, Pro se, Washington, DC.

For Alvin Mathews, Plaintiff: Daniel Adam Osborn, LEAD ATTORNEY, PRO HAC VICE, Osborn Law, P.C., New York, NY; Frank E Piscitelli, Jr, LEAD ATTORNEY, Highland Heights, OH; Philip Jeremy Miller, Osborn Law, P.C., LEAD ATTORNEY, New York, NY; Robert Geoffrey Germany, Pittman Germany, Roberts, Welsh, LLP, Jackson, MS.

For Novartis Pharmaceuticals Corporation, Defendant: Diane E. Lifton, LEAD ATTORNEY, Gibbons P.C. (NY), New York, NY; Joe Gregory Hollingsworth, LEAD ATTORNEY, Donald W Fowler, Spriggs & Hollingsworth, Washington, DC; Katharine R Latimer, Patrick R Harkins, LEAD ATTORNEYS, Hollingsworth LLP, Washington, DC; Megan Beth Gramke, LEAD ATTORNEY, Ulmer & Berne, Cincinnati, OH; Rex A Littrell, LEAD ATTORNEY, Ulmer & Berne - 2, Columbus, OH; Robert E. Johnston, LEAD ATTORNEY, PRO HAC VICE, Hollingsworth, L.L.P., Washington, DC.

JUDGES: WALTER H. RICE, UNITED STATES DISTRICT JUDGE.

OPINION BY: WALTER H. RICE

OPINION

DECISION AND ENTRY OVERRULING DEFENDANT NOVARTIS PHARMACEUTICALS CORPORATION'S MOTION TO EXCLUDE CAUSATION TESTIMONY OF PLAINTIFF'S EXPERTS (DOC. #8-22); SUSTAINING IN PART AND OVERRULING IN PART DEFENDANT NOVARTIS PHARMACEUTICALS CORPORATION'S [*2] MOTION FOR SUMMARY JUDGMENT (DOC. #8-19); SUSTAINING IN PART AND OVERRULING IN PART DEFENDANT NOVARTIS PHARMACEUTICALS CORPORATION'S *DAUBERT* MOTION TO EXCLUDE TESTIMONY OF PLAINTIFF'S EXPERTS DR. SUZANNE PARISIAN, DR. ROBERT MARX, DR. ROBERT FLETCHER, PROFESSOR WAYNE RAY, DR. KEITH SKUBITZ, AND DR. JAMES VOGEL (DOC. #8-18)

Plaintiff Alvin Mathews filed suit against Novartis Pharmaceuticals Corporation ("NPC"), alleging that he developed osteonecrosis of the jaw ("ONJ") after being infused with Aredia® and Zometa®, nitrogenous

bisphosphonate drugs manufactured and marketed by NPC. His Amended Complaint asserts three claims under the Ohio Products Liability Act ("OPLA"), Ohio Revised Code §2307.71, *et seq*., for design defect, inadequate warning, and nonconformance with manufacturer's representation. Doc. # 26.

This matter is currently before the Court on: Defendant NPC's *Daubert* Motion to Exclude Causation Testimony of Plaintiff's Experts, Doc. #8-22; Defendant NPC's Motion for Summary Judgment, Doc. #8-19; and Defendant NPC's *Daubert* Motion to Exclude Testimony of Plaintiff's Experts Dr. Suzanne Parisian, Dr. Robert Marx, Dr. Robert Fletcher, Professor Wayne Ray, Dr. Keith Skubitz, and [*3] Dr. James Vogel, Doc. #8-18.

I. Background and Procedural History

In July of 1998, Plaintiff Alvin Mathews was diagnosed with multiple myeloma with lytic lesions, osteopenia, and significant bone pain. Beginning in January of 1999, his oncologist, Dr. Gregory Gordon, prescribed monthly infusions of Aredia®. Gordon Dep. at 19, 27-28; Ex. 34 to Doc. #8-21. Aredia® and its successor drug, Zometa®, are both manufactured and marketed by NPC. They are approved by the Food and Drug Administration ("FDA"), and have proven very effective in preventing bone pain, fracture and other skeletal complications in patients with cancer that has metastasized to the bone. Exs. 1-3 to Doc. #8-21.

Mathews received Aredia® from January of 1999 through April of 2002, and received Zometa® from May of 2002 through February of 2003. Even though, at that point, Mathews's cancer was in remission, Dr. Gordon resumed monthly infusions of Aredia® as a preventative measure. Mathews continued to receive Aredia® from March of 2003 through mid-2006. Gordon Dep. at 34, 55. Mathews alleges that as a result of taking these drugs, he developed osteonecrosis of the jaw ("ONJ"), a painful, debilitating and disfiguring condition [*4] involving the death of part of the jawbone.

Between December of 2000 and May of 2002, Mathews had several episodes of exposed bone in his jaw. Exs. 43, 45, 46 to Doc. #8-21. In March of 2001, one of his teeth became infected, and he had it extracted. Ex. 44 to Doc. #8-21. Between August of 2004 and March of 2006, he had several cavities filled. He also had root canals on three teeth in his lower right jaw, but the root canals failed. He eventually had those three teeth extracted -- one in January of 2005, one in November of 2005, and one in March of 2006. Exs. 49-55 to Doc. #8-21. In May of 2006, after Mathews complained of pain and swelling in his lower right jaw, his dentist, Dr. Jeffrey Kleinman, referred him to Dr. James Zullinger, an oral surgeon who, in turn, referred him to Dr. Timothy Sorg, an infectious disease specialist. Dr. Sorg diagnosed Mathews with Ludwig's angina, a bacterial infection, and treated him with IV antibiotics. Exs. 56-59 to Doc. #8-21.

In August of 2006, having ruling out dental infection, recurrent Ludwig's angina, and multiple myeloma of the jaw, Dr. Sorg determined that Mathews was suffering from bisphosphonate-induced ONJ. Exs. 58-59 to Doc. #8-21. As [*5] a result, Dr. Gordon stopped the Aredia® treatments. Gordon Dep. at 40. Mathews's pain continued and, on August 21, 2006, pus began draining from his jaw. Dr. Zullinger diagnosed him with an extraoral fistula as a result of the ONJ. Exs. 61-62 to Doc. #8-21. In September of 2006, Mathews again developed an area of exposed bone and was hospitalized for severe jaw pain. He continues to suffer pain, swelling and drainage, and several times each year, Dr. Zuilinger must lance the extraoral fistula. Mathews Dep. at 18.

In December of 2006, Mathews, a resident of Trotwood, Ohio, filed suit against NPC in the United States District Court for the Southern District of New York. His Complaint included common law claims of strict product liability -- design defect, strict product liability -- failure to warn, negligence, breach of express warranty, and breach of implied warranty. His case was one of hundreds of similar cases filed across the country, all alleging that NPC knew or should have known of the risk that Aredia® and Zometa® cause ONJ, and failed to provide timely and adequate notice of that risk to the public and to health care professionals. The Judicial Panel on Multidistrict Litigation [*6] consolidated these cases for pretrial purposes in the United States District Court for the Middle District of Tennessee, and they were then divided into several litigation "waves." *In re Aredia® and Zometa® Products Liability Litigation*, No. 3:06-md-1760 (M.D. Tenn.).

In January of 2012, Mathews's case was remanded to the United States District Court for the Southern District of New York, and in September of 2012, it was transferred to the United States District Court for the Southern District of Ohio. At that time, there were several pending motions, including NPC's motion for summary judgment, Doc. #8-19, and two *Daubert* motions. Does. ##8-18 and 8-22.

In reviewing the pending motions, the Court noted that the parties agreed that Ohio law governed the claims, which are subject to the Ohio Products Liability Act ("OPLA"), Ohio Revised Code §§ 2307.71-2307.80. Because the OPLA abrogates all common law product liability claims, Ohio Revised Code § 2307.71 (B), the Court ordered Mathews to file an Amended Complaint, reasserting his claims under the OPLA. Doc. #23.

The Amended Complaint asserts three claims: (1) strict liability -- design defect under Ohio Revised Code § 2307.75; (2) negligence [*7] -- inadequate warning under Ohio Revised Code § 2307.76(A); and (3) non-conformance with manufacturer's representation under Ohio Revised Code § 2307.77. Before addressing the merits of these claims, the Court turns first to NPC's *Daubert* Motion to Exclude Causation Testimony of Plaintiff's Expert Witness, Dr. Eric Sung. Doc. #8-22.

II. Motion to Exclude Dr. Sung's Expert Witness Testimony (Doc. #8-22)

Citing Federal Rule of Evidence 702 and *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S. Ct. 2786, 125 L. Ed. 2d 469 (1993), Defendant NPC has moved to exclude the testimony of Dr. Eric Sung, Mathews's expert witness on the issue of specific causation, *i.e.*, whether Mathews's use of Aredia® and Zometa® caused him to develop ONJ. Doc. #8-22. After reviewing Mathews's medical and dental records, Dr. Sung concluded, to a reasonable degree of medical certainty, that Mathews developed ONJ due to his treatment with Aredia®. Expert Report at ¶ 18; Ex. 36 to Dec. #8-23. Dr. Sung testified that Mathews developed ONJ "probably around November of 2004, perhaps even earlier." 10/12/11 Sung Dep. at 236; Ex. 2 to Doc. #8-29.

Federal Rule of Evidence 702 governs the admissibility of expert witness testimony. It states:

> A [*8] witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
>
> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
>
> (b) the testimony is based on sufficient facts or data;
>
> (c) the testimony is the product of reliable principles and methods; and
>
> (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702.

In *Daubert*, the Supreme Court assigned the trial judge a "gatekeeping" function. The trial judge must ensure that the expert witness's testimony "both rests on a reliable foundation and is relevant to the task at hand." 509 U.S. at 589. The court need not hold a hearing, but "is required to make an initial assessment of the relevance and reliability of the expert testimony." *Greenwell v. Boatwright*, 184 F.3d 492, 498 (6th Cir. 1999). In the Court's view, there is no need for a hearing in this case because there is enough evidence in the record to allow the Court to determine whether Dr. Sung's proposed expert witness testimony satisfies the *Daubert* [*9] standard.

NPC first argues that Dr. Sung is not qualified to offer an opinion on the subject of specific causation. Sung is a Professor of Clinical Dentistry at UCLA and also maintains a private practice. He has read the relevant medical literature on bisphosphonate-induced ONJ. Since 2001, he has treated approximately twenty patients with bisphosphonate-induced ONJ, and has been indirectly involved in the care of more than twenty other such patients. Sung Report at ¶¶1, 7, 12. In addition, he has co-authored two studies involving bisphosphonate-induced ONJ in rats, and authored an abstract concerning clinical management of ONJ. He has also lectured on this topic. 4/20/11 Sung Dep. at 52, 99-100; Ex. 37 to Doc. #8-23.

NPC acknowledges that Dr. Sung is qualified to *treat and diagnose* patients who have ONJ, but argues that his education and experience do not render him qualified to determine what *caused* ONJ in Mathews's case. As the Sixth Circuit noted in *Tamraz v. Lincoln Electric Co.*, 620 F.3d 665 (6th Cir. 2010), "[t]he ability to diagnose medical conditions is not remotely the same . . . as the ability to deduce . . . in a scientifically reliable manner, the causes of those medical [*10] conditions." *Id.* at 673-74 (quoting *Gass v. Marriott Hotel Servs., Inc.*, 501 F. Supp. 2d 1011, 1019 (W.D. Mich. 2007), *rev'd on other grounds*, 558 F.3d 419 (6th Cir. 2009)).

NPC also cites to *Thomas v. Novartis Pharmaceuticals Corp.*, 443 F. App'x 58, 61-62 (6th Cir. 2011), in which the Sixth Circuit found that the district court had not abused its discretion in excluding specific causation testimony of the plaintiff's treating oral surgeon. The court held that it was not enough for the plaintiff to show that the oral surgeon could "recognize and treat osteonecrosis of the jaw." The plaintiff must also show how the doctor applied his experience and expertise to reach the causation opinion.

Dr. Sung admits that he is not an expert on bisphosphonates. 4/20/11 Sung Dep. at 97-98. However, as the court noted in *Thomas*, "the *Daubert* gate does not auto-

matically slam shut when an individual disclaims being an expert." *Id.* at 61. Therefore, Dr. Sung's statement that he is not an expert on bisphosphonates is not dispositive. The court must independently determine whether Dr. Sung is qualified by virtue of his education and experience. *Id.*

NPC notes that Sung has no demonstrated experience in determining [*11] the cause of ONJ, and has never conducted any research on the alleged link between bisphosphonates and ONJ in humans. Nevertheless, Mathews maintains that Sung is clearly qualified to testify on the topic of specific causation. Sung testified that although he does not hold himself out as an expert, he knows "more than the average dentist" about Aredia® and Zometa®. 4/20/11 Sung Dep. at 97. He has treated many patients with bisphosphonate-induced ONJ and lectured on the topic. As Mathews notes, Sung's experience with other oral conditions allows him to successfully rule out other causes of ONJ. Moreover, although he has not conducted human research on the link between the use of bisphosphonate drugs and ONJ, he has co-authored two studies involving bisphosphonate-induced ONJ in rats.

For these reasons, the Court finds that this case is factually distinguishable from *Thomas*. Based on the evidence in the record, the Court concludes that Dr. Sung's education and experience render him qualified to offer an opinion concerning whether the use of Aredia® and Zometa® caused Mathews to develop ONJ.

NPC also argues that Dr. Sung failed to utilize a reliable methodology to form his specific causation [*12] opinion. Typically, specific causation is determined through the use of a differential etiology, whereby all possible causes are considered and then ruled out one by one until the "most likely cause" is identified. Relevant questions include:

> (1) Did the expert make an accurate diagnosis of the nature of the disease? (2) Did the expert reliably rule in the possible causes of it? (3) Did the expert reliably rule out the rejected causes? If the court answers "no" to any of these questions, the court must exclude the ultimate conclusion reached.

Tamraz, 620 F.3d at 673-74.

NPC maintains that Dr. Sung failed to reliably rule out several potential alternative causes of Mathews's condition. Sung states that he specifically ruled out "cancer, radiation therapy, chemotherapy, corticosteroid therapy, immunotherapy, periodontal disease, dental extractions, intra-oral trauma, diabetes, hypertension, anemia, smoking, alcohol abuse and obesity" as causes of Mathews's ONJ. Sung Report at ¶17. He testified that multiple myeloma would have also been included in his differential etiology. 10/11/11 and 10/12/11 Sung Dep. at 255; Ex. 38 to Doc. #8-23.

NPC argues, however, that Sung has provided no explanation [*13] of *how* he ruled out some of these other possible causes. For example, he admitted at his deposition that he knew of no biopsy that was done to rule out cancer of the jaw. *Id.* at 240. Sung also testified that he ruled out osteomyelitis (an infection of the bone) as a cause of the ONJ, but conceded that Mathews had an obvious infection in his jaw before he developed exposed bone, and that there was no way to determine which came first, the osteomyelitis or the ONJ. *Id.* at 283.

Dr. Sung testified that, although he considered many other causes, "I have to say that list dwindled down to bisphosphonates in a hurry when I looked at it in relationship to when things occurred." *Id.* at 294-95. NPC maintains that Sung's opinion is nothing more than *ipse dixit*; in other words, he simply decided that because Mathews was exposed to bisphosphonates and then developed ONJ, the requisite causation is established. NPC argues that Sung failed to reliably rule out other possible causes, rendering his opinion inadmissible.

The Court disagrees. As the Sixth Circuit held in *Jahn v. Equine Services, PSC*, 233 F.3d 382 (6th Cir. 2000), "[m]edical opinions need not be unchallengeable in order to be admissible." [*14] *Id.* at 393. With respect to causation, "an expert's testimony need not eliminate all other possible causes of the injury." Failure to eliminate other causes may go "to the accuracy of the conclusion," but it does not affect the "soundness of the methodology." *Id.* at 390 (quoting *Ambrosini v. Labarraque*, 101 F.3d 129, 140, 322 U.S. App. D.C. 19 (D.C. Cir. 1996)).

Here, Dr. Sung reviewed Mathews's medical and dental records to determine which possible causes to rule in, and then used reliable methods to rule out those alternative causes out one by one. 10/11/11 Sung Dep. at 96-97, 253, 290. Sung explained that the incidence rate of ONJ is quite high among patients treated with bisphosphonate drugs. *Id.* at 54-55. He testified that the low dose of corticosteroids that Mathews received was unlikely to cause ONJ, and the incidence of ONJ associated with chemotherapy is very rare. *Id.* at 258, 295. Other causes, like tobacco or alcohol abuse, were easily ruled out because they were simply inapplicable. Sung Report ¶18; Mathews Dep. at 71.

In the Court's view, Dr. Sung's specific causation opinion is based on a reliable methodology. Accordingly, the Court overrules NPC's motion to exclude specific

causation testimony [*15] by Mathews's expert witness, Dr. Eric Sung. Doc. #8-22. NPC's objections to the specific methods that Dr. Sung used to rule out alternative causes go only to the weight to be given his testimony, and may be explored further on cross-examination.

III. Motion for Summary Judgment (Doc. #8-19)

When the above-captioned case was transferred to this Court, NPC's Motion for Summary Judgment on all of Mathews's common law claims was already pending. Doc. #8-19. At the Court's request, Mathews filed an Amended Complaint, Doc. #26, which asserts three claims under the Ohio Products Liability Act ("OPLA"), Ohio Revised Code §2307.71, *et seq*. More specifically, Mathews alleges design defect, inadequate warning, and nonconformance with manufacturer's representation. Although the Court gave NPC the opportunity to modify the pending Motion for Summary Judgment in response to the Amended Complaint, NPC informed the Court that no modifications were needed. Doc. #27.

A. Summary Judgment Standard

Summary judgment must be entered "against a party who fails to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof [*16] at trial." *Celotex Corp. v. Catrett*, 477 U.S. 317, 322, 106 S. Ct. 2548, 91 L. Ed. 2d 265 (1986). The moving party always bears the initial responsibility of informing the court of the basis for its motion, and identifying those portions of the record which it believes demonstrate the absence of a genuine issue of material fact. *Id.* at 323; *see also Boretti v. Wiscomb*, 930 F.2d 1150, 1156 (6th Cir. 1991).

"Once the moving party has met its initial burden, the nonmoving party must present evidence that creates a genuine issue of material fact making it necessary to resolve the difference at trial." *Talley v. Bravo Pitino Rest., Ltd.*, 61 F.3d 1241, 1245 (6th Cir. 1995); *see also Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 250, 106 S. Ct. 2505, 91 L. Ed. 2d 202 (1986). Once the burden of production has so shifted, the party opposing summary judgment cannot rest on its pleadings or merely reassert its previous allegations. It is not sufficient to "simply show that there is some metaphysical doubt as to the material facts." *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 586, 106 S. Ct. 1348, 89 L. Ed. 2d 538 (1986). Rule 56 "requires the nonmoving party to go beyond the [unverified] pleadings" and present some type of evidentiary material in support of its position. *Celotex*, 477 U.S. at 324. [*17] "The plaintiff must present more than a scintilla of evidence in support of his position; the evidence must be such that a jury could reasonably find for the plaintiff." *Michigan Prot. & Advocacy Serv., Inc. v. Babin*, 18 F.3d 337, 341 (6th Cir. 1994).

Summary judgment shall be granted "if the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). "Summary judgment will not lie if the dispute about a material fact is 'genuine,' that is, if the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Anderson*, 477 U.S. at 248. In determining whether a genuine dispute of material fact exists, a court must assume as true the evidence of the nonmoving party and draw all reasonable inferences in favor of that party. *Id.* at 255. If the parties present conflicting evidence, a court may not decide which evidence to believe. Credibility determinations must be left to the fact-finder. 10A Wright, Miller & Kane, *Federal Practice and Procedure* Civil 3d § 2726 (1998).

In determining whether a genuine dispute of material fact exists, a court need only consider the materials [*18] cited by the parties. Fed. R. Civ. P. 56(c)(3), "A district court is not . . . obligated to wade through and search the entire record for some specific facts that might support the nonmoving party's claim." *InterRoyal Corp. v. Sponseller*, 889 F.2d 108, 111 (6th Cir. 1989), *cert. denied*, 494 U.S. 1091, 110 S. Ct. 1839, 108 L. Ed. 2d 967 (1990). If it so chooses, however, the court may also consider other materials in the record, Fed. R. Civ. P. 56(c)(3).

B. Analysis

1. Medical Causation

NPC first argues that all of Mathews's claims fail because he has no admissible expert witness testimony establishing that his use of Aredia® and Zometa® caused him to develop ONJ. This argument, however, is foreclosed by the Court's ruling overruling NPC's motion to exclude the specific causation testimony of Dr. Eric Sung.

2. Strict Liability -- Design Defect, Ohio Revised Code § 2307.75

Count I of the Amended Complaint asserts a design defect claim under Ohio Revised Code § 2307.75. The OPLA provides that "a product is defective in design or formulation if, at the time it left the control of its manufacturer, the foreseeable risks associated with its design or formulation . . . exceeded the benefits associated with that design or formulation [*19] . . ." Ohio Revised Code § 2307.75(A). However, a prescription drug "is not defective in design or formulation because some aspect of it is unavoidably unsafe, if the manufacturer . . . pro-

vides adequate warning . . . ." Ohio Revised Code § 2307.75(D).

In Count I of the Amended Complaint, Mathews alleges that Aredia® is defective because its foreseeable risks exceeded the benefits associated with the design or formulation. Mathews further alleges that NPC's warnings about the risk of ONJ are inadequate, and that Aredia® is defective "due to inadequate testing." Am. Compl. ¶¶20-22.

NPC argues that summary judgment is warranted because Mathews cannot show that, at the time the drug left the manufacturer, the foreseeable risks associated with the design exceeded the benefits of that design. Mathews's own oncologist testified that, even after knowing of the risk of ONJ, he continued to prescribe Aredia® to Mathews because the benefits still outweighed the risks. Gordon Dep. at 37-38. NPC further notes that Aredia® was approved by the FDA, the agency charged with weighing a drug's risks and benefits.

Mathews makes no attempt to rebut these arguments, arguing instead only that this claim survives [*20] because of the "issue of dose and duration." Doc. #8-26 at 16. Unfortunately, Mathews does absolutely nothing to explain this statement or to develop this argument. As NPC correctly points out, Mathews identifies no evidence supporting a finding that the drugs were defective based on dose or duration, or that the alleged design defect proximately caused his injury. In fact, the "issue of dose and duration" appears nowhere in the Amended Complaint, and is mentioned nowhere else in Mathews's Memorandum in Opposition to Defendant's Motion for Summary Judgment.

Based on the evidence presented, no reasonable jury could find in favor of Mathews on his design defect claim.[1] The Court therefore sustains NPC's motion for summary judgment on Count I of the Amended Complaint.

> 1 Citing Ohio Revised Code § 2307.75(D), NPC further argues that summary judgment is warranted because the warnings it gave were adequate. Because Mathews has failed to present sufficient evidence from which a reasonable jury could find that the foreseeable risks of the drugs exceeded the benefits, the Court need not address the adequacy of the warnings in the context of the design defect claim.

3. Inadequate Warning, Ohio Revised Code § 2307.76(A)

Count [*21] II of the Amended Complaint asserts a claim of inadequate warning under Ohio Revised Code § 2307.76(A). Mathews alleges that NPC knew or should have known that Aredia® creates an unreasonable risk of ONJ, that NPC breached its duty to exercise reasonable care by failing to warn his prescribing physicians and the dental community about that risk, and that this was the proximate cause of his injury. Am. Compl. ¶¶30-33,

The OPLA provides that a product is defective due to inadequate warning if, when it left the manufacturer's control, both of the following applied:

> (a) The manufacturer knew or, in the exercise of reasonable care, should have known about a risk that is associated with the product and that allegedly caused harm for which the claimant seeks to recover compensatory damages; [and]
>
> (b) The manufacturer failed to provide the warning or instruction that a manufacturer exercising reasonable care would have provided concerning that risk, in light of the likelihood that the product would cause harm of the type for which the claimant seeks to recover compensatory damages and in light of the likely seriousness of that harm.

Ohio Rev. Code § 2307.76(A)(1).

A product is defective due to [*22] inadequate *post-marketing* warning if, at a relevant time after it left the manufacturer's control, both of the following applied:

> (a) The manufacturer knew or, in the exercise of reasonable care, should have known about a risk that is associated with the product and that allegedly caused harm for which the claimant seeks to recover compensatory damages; [and]
>
> (b) The manufacturer failed to provide the post-marketing warning or instruction that a manufacturer exercising reasonable care would have provided concerning that risk, in light of the likelihood that the product would cause harm of the type for which the claimant seeks to recover compensatory damages and in light of the likely seriousness of that harm.

Ohio Rev. Code § 2307.76(A)(2).

To succeed on an "inadequate warning" claim, a plaintiff must prove: "(1) a duty to warn against reasonably foreseeable risks; (2) breach of this duty; and (3) an

injury that is proximately caused by the breach." *Miller v. ALZA Corp.*, 759 F. Supp.2d 929, 934 (S.D. Ohio 2010) (quoting *Graham v. Am. Cyanamid Co.*, 350 F.3d 496, 514 (6th Cir. 2003)).

The first element is not in dispute. NPC argues that it is entitled to summary judgment on this claim because [*23] Mathews cannot show that NPC breached a duty to warn against reasonably foreseeable risks, or that his injury was proximately caused by the breach. Based on the evidence presented, the Court finds that genuine issues of material fact preclude summary judgment on this claim.

(a) Duty

NPC correctly notes that there is no duty to warn of a risk that is unknown and unknowable. *Bartel v. John Crane, Inc.*, 316 F. Supp.2d 603, 611-12 (N.D. Ohio 2004). NPC maintains that it issued appropriate warnings as soon as it became aware of the risk of bisphosphonate-induced ONJ. NPC notes that it was not until September of 2003 that Dr. Richard Marx published the first case reports linking bisphosphonate drugs to ONJ. R.E. Marx, *Pamidronate (Aredia) and Zoledronate (Zometa) Induced A vascular Necrosis of the Jaws: A Growing Epidemic*, 61 J. Oral Maxillofacial Surg. 1115 (2003). That same month, NPC voluntarily changed its labels to note that cases of ONJ had been reported since the drugs were introduced on the market. The label revision stated, however, that ONJ "has other well documented risk factors, It is not possible to determine if these events are related to Zometa or other bisphosphonates, to concomitant [*24] drugs or other therapies." Ex. 24 to Dec. #8-21.

NPC revised its labels again in February of 2004 to note that, because most cases of bisphosphonate-induced ONJ appeared to be related to a dental procedure, dental surgery was not advisable. Ex. 27 to Dec. #8-21. In September of 2004, NPC again revised the labels to state that patients being treated with bisphosphonates "should avoid invasive dental procedures if possible." Ex. 28 to Doc. #8-21. That same month, NPC sent letters to doctors warning of the risk of bisphosphonate-induced ONJ. Ex. 32 to Doec. #8-21. In May of 2005, NPC sent similar letters to dentists and oral surgeons. Ex. 18 to Doc. #8-21.

Mathews maintains that these warnings were neither timely nor adequate. He notes that a 1981 study involving rats had shown a connection between bisphosphonates and ONJ. Ex. 23 to Vecchione Decl. filed in *In re: Aredia and Zometa Prods. Liab. Litig.*, 3:06-md-1760 (M.D. Tenn.) [Doc. #54661. Moreover, at least six cases of ONJ were allegedly reported during the 1991 clinical trials of Aredia®. Exs. 20, 26-27 to Vecchione Decl. Mathews therefore maintains that NPC should have identified the risk no later than 1991. Nevertheless, NPC issued [*25] no warnings at all until September of 2003. Mathews maintains that the warnings given thereafter were inadequate.

Notably, in "Wave I" of the multi-district litigation, the MDL Court determined that genuine issues of material fact preclude summary judgment on the issue of warning adequacy. It found that there are genuine factual disputes concerning *what* NPC knew or should have known and *when*, and whether the letters sent to doctors and dentists were timely and adequately conveyed information about the risk of developing ONJ. *In re Aredia and Zometa Prods. Liability Litigation*, No. 3:06-md-1760, Docs. #2766, 2767 (M.D. Tenn. Aug. 13, 2009). Finding no basis for disturbing the ruling of the MDL Court on this issue, the Court concludes that genuine issues of material fact preclude summary judgment on the question of whether NPC breached its duty to provide adequate warnings concerning the risk of bisphosphonate-induced ONJ.[2]

> 2 Under the "law of the case" doctrine, this court cannot reconsider issues decided at an earlier stage of the proceedings. *McKenzie v. BellSouth Telecommunications, Inc.*, 219 F.3d 508, 512 (6th Cir. 2000). Exceptions exist "(1) where substantially different evidence [*26] is raised on subsequent trial; (2) where a subsequent contrary view of the law is decided by the controlling authority; or (3) where a decision is clearly erroneous and would work a manifest injustice." *Hanover Ins. Co. v. Am. Eng'g Co.*, 105 F.3d 306, 312 (6th Cir. 1997). None of those exceptions is present herein.

There is, however, one Ohio-specific duty-related issue raised by the parties that was not addressed by the MDL court. The "learned intermediary" defense, as set forth in the OPLA, provides that:

> An ethical drug is not defective due to inadequate warning or instruction if its manufacturer provides otherwise adequate warning and instruction *to the physician or other legally authorized person who prescribes or dispenses that ethical drug* for a claimant in question and if the federal food and drug administration has not provided that warning or instruction relative to that ethical drug is to be given directly to the ultimate user of it.

Ohio Rev. Code § 2307.76(C) (emphasis added). Since this statute refers only to physicians or other legally authorized persons who prescribe or dispense the drug in question, there is some question about whether NPC also has a duty to warn dentists [*27] and oral surgeons of the risks of bisphosphonate-induced ONJ.[3]

> 3 Although NPC did eventually send warning letters to dentists and oral surgeons, it did not do so until May of 2005.

Mathews notes that Restatement (Third) of Torts provides:

> A prescription drug or medical device is not reasonably safe due to inadequate instructions or warnings if reasonable instructions or warnings regarding foreseeable risks of harm are not provided to: (1) prescribing *and other health-care providers who are in a position to reduce the risks of harm in accordance with the instructions or warnings. . .*

Restatement (Third) of Torts: Prod. Liab. § 6(d)(1) (1998) (emphasis added). Mathews maintains that because bisphosphonate-induced ONJ is often triggered by invasive dental procedures, and because dentists and oral surgeons are in the best position to reduce the risk of harm, drug manufacturers have a duty to warn them of the relevant risks.

Ohio has not expressly adopted this section of the Restatement (Third) of Torts. Even so, Ohio Revised Code § 2307.76(A) refers to the failure to provide "the warning or instruction that a manufacturer exercising reasonable care would have provided concerning that risk, in [*28] light of the likelihood that the product would cause harm of the type for which the claimant seeks to recover compensatory damages and in light of the likely seriousness of that harm."

In the Court's view, the question of whether the manufacturer exercised "reasonable care" encompasses both the *content* of that warning and the *method* by which the manufacturer disseminates that warning. *See Seley v. G.D. Searle & Co.*, 67 Ohio St.2d 192, 198, 423 N.E.2d 831, 837 (Ohio 1981) ("The fact finder may find a warning to be unreasonable, hence inadequate, in its factual content, its expression of the facts, or the method or form in which it is conveyed."); *Thom v. Bristol-Myers Squibb Co.*, 353 F.3d 848, 853 (10th Cir. 2003) (noting that one of the factors to be considered in determining whether a warning is adequate is what means were used to convey it). In determining whether the manufacturer exercised "reasonable care" in issuing a warning, a jury could find that, because bisphosphonate-induced ONJ is often triggered by invasive dental procedures, NPC had a duty to warn not only the prescribing physicians, but also the dental care providers who are, arguably, in an even better position to prevent [*29] the alleged harm.[4]

> 4 The question of whether a manufacturer exercised reasonable care in issuing a warning is distinct from the question of whether a manufacturer has discharged its duty to warn by providing an adequate warning to a learned intermediary. Therefore, the fact that the "learned intermediary" defense, codified in Ohio Revised Code § 2307.76(C), appears to apply only when a warning is given to the *prescribing physician*, does not mean that, under certain circumstances, a manufacturer's *duty to warn* may extend to other health care professionals as well. The Court expresses no opinion, at this juncture, about whether the "learned intermediary" defense could be extended to apply to warnings given to health care providers other than the prescribing physician.

For the reasons set forth above, and those previously expressed by the MDL court in the "Wave I" cases, the Court concludes that genuine issues of material fact preclude summary judgment on the question of whether NPC breached its duty to provide timely and adequate warnings concerning the risk of bisphosphonate-induced ONJ.

(b) Proximate Causation

NPC also argues that Mathews has failed to produce sufficient evidence that the [*30] alleged inadequate warning proximately caused his injury. In *Seley*, the Ohio Supreme Court explained that, in the context of a "failure to warn" claim, proximate cause involves two sub-issues: "(1) whether lack of adequate warnings contributed to the plaintiff's [use] of the drug, and (2) whether [use] of the drug constitutes a proximate cause of the plaintiff's injury." 67 Ohio St.2d at 200, 423 N.E.2d at 838. NPC argues that Mathews's claim is deficient in both respects.

NPC first argues that Mathews cannot prove that the lack of an adequate warning contributed to his use of Aredia®. Under Ohio law, it is presumed that if an adequate warning is given, it will be read and heeded. But where no warning is given, or where an inadequate warning is given, a rebuttable presumption arises that the failure to adequately warn was a proximate cause of the plaintiff's use of the drug. *Id.*

This presumption may be rebutted by proof that "an adequate warning would have made no difference in the

physician's decision as to whether to prescribe a drug or as to whether to monitor the patient thereafter." *Id.* at 201, 423 N.E.2d at 838. Where a treating physician unequivocally testifies that an adequate [*31] warning would not have altered the course of treatment, summary judgment is warranted. However, if the evidence does not affirmatively establish that the physician "would not have behaved differently had he received a different warning," the proximate cause issue is best left to the jury. *Miller*, 759 F. Supp.2d at 936 (quoting *Williams v. Lederle Labs.*, 591 F. Supp. 381, 387 (S.D. Ohio 1984)).

NPC notes that Dr. Gordon, Mathews's oncologist, testified that even after he learned of the alleged connection between bisphosphonate drugs and ONJ, he still continued to prescribe Aredia® for Mathews because the benefits outweighed the risks. Gordon Dep. at 37-38; Ex. 34 to Doc. #8-21. NPC contends that Gordon's testimony is sufficient to rebut the presumption, and to warrant summary judgment on this claim.

Mathews maintains that Gordon's testimony is not necessarily dispositive. Quoting *In re: Aredia and Zometa Products Liability Litigation (White)*, 3:06-cv-550, Doc. #322 (M.D. Tenn. Aug. 13, 2009), he argues that, he can still withstand summary judgment by showing that "Plaintiff himself and/or Plaintiff's dentist or oral surgeon might have behaved differently." Mathews notes that Dr. Gordon [*32] also testified that had he known of the risk of ONJ, he would have: (1) discussed it with Mathews; and (2) stopped the bisphosphonate treatments for two or three months before Mathews had any invasive dental procedures. Gordon Dep. at 54; Ex. F to Doc. #8-26. The first is significant; the second is not.

Mathews testified that if Dr. Gordon had told him that Aredia® might cause ONJ, he would have refused to take it, despite his doctor's recommendation. According to Mathews, at the very least, he would not have even considered taking Aredia® unless and until he actually developed skeletal complications from his cancer. Mathews Dep. at 109-10; Ex. K to Doc. #8-26.

NPC maintains that Mathews's testimony is speculative and self-serving and should be disregarded. The Court disagrees. The Court cannot resolve credibility issues on a motion for summary judgment. In the Court's view, Mathews's deposition testimony is sufficient to create a genuine issue of material fact about whether his use of the drug was caused by the allegedly inadequate warning. A reasonable jury could find that if NPC had disclosed the risk of ONJ, Dr. Gordon would have discussed the risk with Mathews, and Mathews would [*33] have refused to take Aredia®, thereby altering his course of treatment.

Having found that Mathews's deposition testimony is sufficient to withstand summary judgment on this portion of the proximate cause issue, the Court need not address his alternate argument that if Dr. Gordon had known of the risk of ONJ, he would have stopped the bisphosphonate treatments for two or three months before Mathews had any invasive dental procedures. Nevertheless, the Court notes that Mathews has no presented no evidence to support a finding that a "drug holiday" would have averted the injury.[5]

> 5 Mathews also argues that if his dental care providers had known of the risk of ONJ, they may have opted for alternative treatments rather than extracting his teeth. As NPC notes, however, Dr. Sung testified that Mathews developed ONJ in 2004, prior to the date of the extractions at issue. 10/12/11 Sung Dep. at 236; Ex. 2 to Doc. #8-29. This makes it very difficult for Mathews to show that a warning to avoid invasive dental procedures would have averted the injury.

The second sub-issue with respect to proximate cause is "whether [use] of the drug constitutes a proximate cause of the plaintiff's injury." *Seley*, 67 Ohio St.2d at 200, 423 N.E.2d at 838. [*34] NPC maintains that because Mathews has no admissible expert witness testimony on the issue of specific causation, summary judgment is appropriate. Again, this argument is foreclosed by the Court's decision overruling NPC's motion to exclude Dr. Sung's expert witness testimony.

The Court finds that genuine issues of material fact exist concerning whether the allegedly inadequate warning was the proximate cause of Mathews's injury. The Court therefore overrules NPC's motion for summary judgment on Count II of the Amended Complaint.

4. Nonconformance with Manufacturer's Representations, Ohio Revised Code § 2307.77

In Count III of the Amended Complaint, Mathews alleges that NPC "expressly warranted, by and through statements made by Defendant or its authorized agents, that Aredia was safe, effective, and fit for its intended use," Am. Compl. ¶35. He further alleges that the drug did not conform to this warranty "because it caused serious adverse side effects, including osteonecrosis of the jaw." *Id.* at 137.

Ohio Revised Code § 2307.77 provides that "[a] product is defective if it did not conform, when it left the control of its manufacturer, to a representation made by that manufacturer." [*35] A "representation" is defined as an "express representation of a material fact concerning the character, quality, or safety of a product." Ohio Revised Code § 2307.71(A)(14).

To recover under this section of the OPLA, a plaintiff must prove:

> 1) that the manufacturer made a representation as to a material fact concerning the character or quality of the manufacturer's product;
> 2) that the product did not conform to that representation;
> 3) that the plaintiff justifiably relied on that representation; and
> 4) that the plaintiff's reliance on the representation was the direct and proximate cause of the plaintiff's injuries.

Gawloski v. Miller Brewing Co., 96 Ohio App.3d 160, 165, 644 N.E.2d 731, 734 (Ohio Ct. App. 1994).

NPC argues that summary judgment is appropriate because, based on the evidence presented, Mathews cannot prove that NPC made an express representation as to any material fact concerning the character or quality of Aredia® and Zometa®. The Court agrees. Outside the bare allegations contained in the Amended Complaint, Mathews has not identified *any* express representation made by NPC -- on the drug labels, in any advertising, or in any oral communications to Mathews or his health [*36] care professionals -- on which he or his doctors relied. In his Memorandum in Opposition to NPC's Motion for Summary Judgment, he argues only that "[a] drug warranted to help bones destroyed [his] jaw bone," Doc. # 8-26, at 17.

In response to NPC's motion, Mathews cites to *Knipe v. SmithKline Beecham*, 583 F. Supp.2d 602 (E.D. Pa. 2008), in support of his argument that summary judgment is not appropriate on this claim. That case, however, is inapposite for two reasons. First, it involved a breach of express warranty claim under New Jersey law. Second, unlike Mathews, the plaintiff in that case did identify specific representations made by the drug manufacturer concerning the safety and effectiveness of the drug at issue. *See id.* at 624 ("Plaintiff has referenced several public representations by GSK or by researchers, seemingly connected with GSK, which could possibly form the basis of the claimed 'off-label' promotion" of the drug for pediatric use).

Here, because Mathews has identified no express representation made by NPC, and has pointed to no evidence to substantiate his allegation that NPC "expressly warranted . . . that Aredia was safe, effective, and fit for its intended use," [*37] summary judgment is warranted on this claim. *See Krumpe/back v. Breg, Inc.*, 491 Fed. Appx. 713, 722 (6th Cir. 2012) (interpreting Ohio Revised Code § 2307.77), The Court therefore sustains NPC's motion for summary judgment on Count Ill of the Amended Complaint.

IV. *Daubert* Motion to Exclude Testimony of Plaintiff's Experts Dr. Suzanne Parisian, Dr. Robert Marx, Dr. Robert Fletcher, Professor Wayne Ray, Dr. Keith Skubitz, and Dr. James Vogel (Doc. #8-18)

In the MDL Court, Defendant NPC also filed a *Daubert* Motion to Exclude Testimony of Plaintiff's Experts Dr. Suzanne Parisian, Dr. Robert Marx, Dr. Robert Fletcher, Professor Wayne Ray, Dr. Keith Skubitz, and Dr. James Vogel. Doc. #8-18. The motion was filed in connection with all of the "Wave Ill" cases, and it incorporated by reference all previous motions and briefs filed in the previous "Waves" of litigation. Neither the MDL Court nor the United States District Court for the Southern District of New York ruled on the pending motion before the case was transferred to this Court.

During a conference call held on September 9, 2013, counsel for the parties agreed that Mathews would not be relying on the testimony of Dr. Robert Fletcher. The [*38] motion is, therefore, moot as to Dr. Fletcher. With respect to the other five case-wide expert witnesses, the parties agreed to be bound by this Court's rulings on the *Daubert* motions that were filed in two other MDL cases transferred to this Court, *Bowles v. Novartis Pharmaceuticals Corporation*, Case No. 3:12-cy-145, and *Sheffer v. Novartis Pharmaceuticals Corporation*, Case No. 3:12-cv-238.

On September 20, 2013, the Court issued a Decision and Entry Sustaining in Part and Overruling in Part Defendant NPC's *Daubert* Motions to Exclude Plaintiffs' Expert Witness Testimony in *Bowles* and *Sheffer*. Doc. #65 in Case No. 3:12-cv-145, and Doc. #61 in Case No. 3:12-cv-238. That Decision and Entry is attached as Exhibit 1 to this document, and is incorporated by reference. As agreed, Mathews's expert witnesses will be bound by the general holdings contained in that Decision and Entry.

During the September 9, 2013, conference call, it was agreed that the parties would file supplemental memoranda addressing any arguments specific to Mathews's case. NPC has made two case-specific arguments. First, it argues that Drs. Marx, Vogel, and Skubitz should not be permitted to testify about the benefits of [*39] pretreatment dental screening and avoiding invasive dental procedures, because those opinions do not "fit" the facts of this case and are, therefore, irrelevant. NPC maintains that there is no evidence that a dental screening done before Mathews began his Aredia® treatments in 1999 would have detected any problems or changed the course of treatment. It further argues that because Mathews's ONJ developed spontaneously, and

not as the result of any extractions, a warning to avoid invasive dental procedures would not have made any difference. Moreover, by the time Mathews had his teeth extracted in 2005 and 2006, the package inserts already included warnings about avoiding invasive dental procedures. NPC further argues that there were no viable alternatives to extracting the teeth at issue. Kleinman Dep. at 25-26, 54-55; Ex. 48 to Doc. #8-21,

Second, NPC argues that Dr. Vogel and Dr. Skubitz should not be permitted to testify about alternative, reduced dosing schedules for the drugs. It contends that, because the "Corso study" on which the doctors rely was not published until 2007, after Mathews ceased his bisphosphonate treatments, that study cannot support an opinion that Mathews should [*40] have been on a different dosing schedule.

Although Mathews was given an opportunity to respond to these case-specific arguments, he filed nothing to rebut them, impliedly conceding that the expert witness opinions on these topics are inapplicable. Based on the evidence presented, the Court agrees with NPC that expert witness testimony concerning the benefits of pretreatment dental screening and avoiding invasive dental procedures, and expert witness testimony about alternative, reduced dosing schedules is irrelevant to the facts of this particular case. As such, Mathews's expert witnesses will not be permitted to testify concerning these topics.

For the reasons set forth in the Court's September 20, 2013, Decision and Entry in *Bowles* and *Sheffer*, Doc. #65 in Case No. 3:12-cv-145, and Doc. #61 in Case No. 3:12-cv-238, and the reasons discussed herein, the Court sustains in part and overrules in part Defendant NPC's *Daubert* Motion to Exclude Testimony of Plaintiff's Experts Dr. Suzanne Parisian, Dr. Robert Marx, Dr. Robert Fletcher, Professor Wayne Ray, Dr. Keith Skubitz, and Dr. James Vogel, Doc. #8-18.

V. Conclusion

For the reasons set forth above, the Court:

(1) OVERRULES Defendant NPC's [*41] *Daubert* Motion to Exclude Causation Testimony of Plaintiff's Experts, Doc. #8-22;

(2) SUSTAINS IN PART and OVERRULES IN PART Defendant NPC's Motion for Summary Judgment, Doc. #8-19, (summary judgment is granted as to Counts I and III of the Amended Complaint); and

(3) SUSTAINS IN PART AND OVERRULES IN PART Defendant NPC's *Daubert* Motion to Exclude Testimony of Plaintiff's Experts Dr. Suzanne Parisian, Dr. Robert Marx, Dr. Robert Fletcher, Professor Wayne Ray, Dr. Keith Skubitz, and Dr. James Vogel, Doc. #8-18.

Date: October 24, 2013

/s/ Walter H. Rice

WALTER H. RICE

UNITED STATES DISTRICT JUDGE

EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT FOR THE SOUTHERN DISTRICT OF OHIO

WESTERN DIVISION

BARBARA BOWLES,

Plaintiff,

v.

NOVARTIS PHARMACEUTICALS CORPORATION,

Defendant

SHIRLEY E. SHEFFER, *et al.*,

Plaintiffs,

v.

NOVARTIS PHARMACEUTICALS CORPORATION,

Defendant

Case No. 3:12-cv-145

JUDGE WALTER H. RICE

Case No. 3:12-cv-238

JUDGE WALTER H. RICE

DECISION AND ENTRY SUSTAINING IN PART AND OVERRULING IN PART: (1) DEFENDANT'S MOTIONS TO EXCLUDE TESTIMONY OF PLAINTIFF'S EXPERT DR. KEITH SKUBITZ (DOC. #30 IN CASE NO. 3:12-cv-145 and DOC. #31 IN CASE NO, 3:12-cv-238); (2) DEFENDANT'S MOTIONS TO EXCLUDE TESTIMONY OF PLAINTIFF'S [*42] EXPERT DR. JAMES VOGEL (DOC. #31 IN CASE NO. 3:12-cv-145 and DOC. #33 IN CASE NO. 3:12-cv-238); (3) DEFENDANT'S MOTIONS TO EXCLUDE TESTIMONY OF PLAINTIFF'S EXPERT DR. SUZANNE PARISIAN (DOC. #32 IN CASE NO, 3:12-cv-145 and DOC. #34 IN CASE NO. 3:12-cv-238); (4) DEFENDANT'S MOTIONS TO EXCLUDE TESTIMONY OF PLAINTIFF'S EXPERT PROFESSOR WAYNE RAY (DOC. #33 IN CASE NO. 3:12-cv-145 and DOC. #35 IN CASE NO. 3:12-cv-2381; AND (5) DEFENDANT'S MOTION TO EXCLUDE TESTIMONY OF PLAINTIFF'S EXPERT DR. ROBERT MARX ((DOC, #35 IN

CASE NO. 3:12-cv-145 and DOC. #36 IN CASE NO. 3:12-cv-238)

Plaintiffs in the above-captioned cases allege that they developed osteonecrosis of the jaw ("ONJ") as a result of receiving infusions of Defendant's bisphosphonate drugs, Aredia® and Zometa.® This matter is currently before the Court on numerous motions filed by Defendant, Novartis Pharmaceuticals Corporation ("NPC"), seeking to exclude the testimony of Plaintiffs' retained expert witnesses Dr. Keith Skubitz, Dr. James Vogel, Dr. Suzanne Parisian, Professor Wayne Ray, and Dr. Robert Marx.

I. Background

Defendant NPC manufactures, markets and distributes the bisphosphonate drugs Aredia® and Zometa.® These intravenous drugs [*43] are approved by the Food and Drug Administration ("FDA"), and routinely prescribed to cancer patients whose cancer has metastasized to the bone. They have proven effective in preventing bone pain, fractures and other skeletal complications. Despite their significant benefits, Aredia® and Zometa® allegedly also cause osteonecrosis of the jaw ("ONJ"), or death of a portion of the jawbone, in a significant number of patients.

After Plaintiff Barbara Bowles was diagnosed with multiple myeloma in 1997, her oncologist prescribed monthly infusions of Aredia®. In July of 2001, after having a tooth extracted, she experienced significant jaw problems, including a wound that would not heal, pus drainage, an unpleasant odor, and jaw pain. In July of 2006, Bowles was diagnosed with ONJ, which was allegedly caused by the Aredia®. This prompted her oncologist to discontinue the Aredia® treatments.

Plaintiff Shirley Sheffer was diagnosed with breast cancer in May of 2005. Her oncologist prescribed Zometa®, which is Aredia's® successor drug. In March of 2006, her dentist found that one of Sheffer's teeth was infected and part of her jawbone was exposed. He referred her to specialists, who diagnosed ONJ, [*44] allegedly caused by the Zometa®. She had the infected tooth extracted and, several months later, had another tooth extracted. She has been plagued with infection and pain since then. In 2008, her jaw broke at the site of the first extraction.

Both Plaintiffs filed suit against NPC in the United States District Court for the District of Columbia, asserting various product liability claims. The United States Judicial Panel on Multidistrict Litigation ("MDL") consolidated their cases for pretrial purposes in the United States District Court for the Middle District of Tennessee, along with hundreds of similar cases that had been filed nationwide. *In re: Aredia and Zometa Products Liability Litigation*, No. 3:06-md-1760 (M.D. Tenn.). Those cases were subdivided into several litigation "waves" and ultimately remanded to the transferor courts. Plaintiffs' cases are both part of "Wave III." Because both Plaintiffs are residents of Ohio, their cases were later transferred to this district for further proceedings.

In connection with its Motions for Summary Judgment in the above-captioned cases, NPC has moved to exclude or limit the testimony of several of Plaintiffs' expert witnesses. Notably, [*45] these are case-wide witnesses, having been retained to testify on behalf of the plaintiffs in nearly all of the MDL cases against NPC. Prior to remanding the cases to the transferor courts, the MDL Court issued several rulings concerning these expert witnesses. Those decisions constitute the "law of the case," and will not be revisited.[1] *See Deutsch v. Novartis Pharmaceuticals Corp.*, 768 F. Supp.2d 420, 428-29 (E.D.N.Y. 2011) (noting that reversing decisions made by the MDL Court would lead to inconsistent pretrial rulings and would undermine the purpose of the Multi District Litigation Act).

1 Under the "law of the case" doctrine, this court cannot reconsider issues decided at an earlier stage of the proceedings. *McKenzie v. BellSouth Telecommunications, Inc.*, 219 F.3d 508, 512 (6th Cir. 2000). Exceptions exist "(1) where substantially different evidence is raised on subsequent trial; (2) where a subsequent contrary view of the law is decided by the controlling authority; or (3) where a decision is clearly erroneous and would work a manifest injustice." *Hanover Ins. Co. v. Am. Eng'g Co.*, 105 F.3d 306, 312 (6th Cir. 1997).

Once the MDL Court remanded the cases to the transferor courts, [*46] NPC filed motions to exclude and to further limit the testimony of these expert witnesses. As Plaintiffs note, although some transferor courts have limited a portion of the expert witness testimony, virtually no court has completely excluded the testimony of any of these witnesses. In the above-captioned cases, as it has in the other transferor courts, NPC generally challenges the qualifications and the methodology of the expert witnesses. NPC also makes several case-specific objections, arguing that some of the expert witness testimony simply does not fit the facts of these two cases.

II. Legal Standard for Admissibility Under Federal Rule of Evidence 702 and *Daubert*

The admissibility of expert witness testimony is governed by Federal Rule of Evidence 702. That rule states:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
>
> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
>
> (b) the testimony is based on sufficient facts or data;
>
> (c) the testimony is the product of reliable principles [*47] and methods; and
>
> (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702.

In *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S. Ct. 2786, 125 L. Ed. 2d 469 (1993), the Supreme Court assigned the trial judge a "gatekeeping" function. The trial judge must ensure that the expert witness's testimony "both rests on a reliable foundation and is relevant to the task at hand." *Id.* at 589. The Court need not hold a hearing, but "is required to make an initial assessment of the relevance and reliability of the expert testimony." *Greenwell v. Boatwright*, 184 F.3d 492, 498 (6th Cir. 1999).

As previously noted, many other transferor courts have already addressed nearly identical motions filed by NPC in the other MDL cases, and several of those courts have held *Daubert* hearings. Because this Court has the benefit of those previous decisions and several transcripts, it sees no need for any additional *Daubert* hearings.

III. Expert Witnesses

A. Dr. Keith Skubitz

Dr. Keith Skubitz is an oncologist on the faculty at the University of Minnesota. The MDL Court has already determined that Dr. Skubitz is qualified as an expert witness to testify about general causation, *i.e.*, whether [*48] Aredia® and Zometa® cause ONJ, and about the medical accuracy of the warnings given by NPC. NPC acknowledges that this is the law of the case. The MDL Court, however, did not consider the admissibility of Dr. Skubitz's opinions concerning alternative dosing intervals or the benefit of pretreatment dental screening. *In re Aredia & Zometa Products Liability Litigation*, No. 3:06-md-1760, Doc. #2810, (M.D. Tenn. Aug. 13, 2009).

NPC now seeks to exclude Dr. Skubitz's testimony concerning: (1) alternative dosing intervals; (2) the benefit of pretreatment dental screening; (3) the drafting and approval of the Aredia® and Zometa® labels; and (4) the inclusion of the incidence rate of ONJ in the Aredia® and Zometa® labels. NPC argues that Dr. Skubitz is not qualified to offer an opinion on these topics.

1. Alternative Dosing Intervals

In Section V of his rebuttal expert witness report, Dr. Skubitz opines that alternative dosing schedules may be just as effective as the ongoing monthly infusions suggested by NPC, and would reduce the risk of ONJ. He gives his own patients monthly infusions of Zometa® for 10 months, and then reduces the frequency of the infusions. With some patients, he terminates [*49] bisphosphonate therapy altogether after two years. He notes that, in doing so, he has not seen a noticeable increase in the rate of skeletal events. Ex. 4 to Doc. #30 in Case No. 12-cv-145. He admitted, however, that it is possible that the reduced dosing is not as effective as the ongoing infusions recommended by NPC. Skubitz Dep. at 332 (Ex. 3 to Doc. #30 in Case No. 12-cv-145).

NPC argues that Dr. Skubitz's opinion is nothing but *ipse dixit*, and is inadmissible. It notes that in *Deutsch v. Novartis Pharmaceuticals Corp.*, 768 F. Supp.2d 420, 447 (E.D.N.Y. 2011), the transferor court held that, to the extent Dr. Skubitz's opinion was based solely on his personal observations of his own patients, and was not supported by any data, it was inadmissible. Dr. Skubitz, however, also bases his opinion on the "Corso study," which found that reducing the dose of Zometa® to once every three months, after one year of monthly infusions, reduces the risk of ONJ without decreasing the effectiveness of the drug. *See A. Corso et al., A Different Schedule of Zoledronic Acid Can Reduce the Risk of the Osteonecrosis of the Jaw in Patients with Multiple Myelmna*, 21 Leukemia 1545, 1548 (2007). Ex. 5 to [*50] Doc. #30 in Case No. 12-cv-145.

NPC argues that the Corso study is not scientifically reliable because there was no control group, and it is not clear whether the patients in that study had conditions that satisfy Dr. Skubitz's definition of ONJ. The court in *Deutsch* rejected these arguments, finding that the lack of a control group goes to the weight of the testimony, not

to its admissibility, and that study's lack of a precise definition of ONJ is not a fatal flaw. Therefore, to the extent that Dr. Skubitz's opinion about alternative dosing was premised on relevant medical literature, the court found it to be admissible. 768 F. Supp.2d at 446-47. This Court agrees with the *Deutsch* court's reasoning with respect to the reliability of Dr. Skubitz's opinion about alternative dosing.

The question remains, however, whether his opinion is relevant to the remaining claims in either of the above-captioned cases. As NPC notes, because Sheffer developed ONJ within one year after beginning Zometa® treatments, and ceased treatment immediately after she was diagnosed with ONJ, Dr. Skubitz's proposed alternative dosing schedule does not appear to apply to her at all. Sheffer has made no effort to [*51] respond to this argument. Because the Court finds that she has failed to demonstrate that Dr. Skubitz's testimony on this topic is relevant to her claims, it is inadmissible in her case.

In contrast, because Bowles received monthly infusions of Aredia® for several years before developing ONJ, Dr. Skubitz's testimony appears to be relevant to her situation. NPC argues, however, that because the Corso study, on which Dr. Skubitz bases his opinion, was published *after* Bowles ceased Aredia® treatments, it does not support a finding that Bowles should have been on a different dosing schedule. If, during the time period that Bowles was receiving Aredia®, no evidence existed that a reduced dosing schedule would be just as effective and less risky, Dr. Skubitz's testimony on this topic is irrelevant. Again, Bowles completely fails to respond to this argument. Since Bowles has failed to show that Dr. Skubitz's testimony is relevant to her claims, it is inadmissible.

2. Benefit of Pretreatment Dental Screening and Stronger Warnings

Dr. Skubitz also opines that pretreatment dental screenings and strong warnings about avoiding invasive dental procedures are beneficial in reducing the risk of ONJ. [*52] Report, at ¶126 (Ex. 2 to Doc. #30 in Case No. 3:12-cv-145). NPC maintains that this testimony is irrelevant and inadmissible because there is no evidence that such measures would have made any difference in Plaintiffs' cases.

Bowles's problems began after she had a tooth extracted in 2001. Her dentist testified that because the tooth was so deeply decayed, extraction was the only option. Mazzola Dep. at 62; Ex. 11 to Doc. #35 in Case No. 3:12-cv-145. As the Court noted, however, in ruling on NPC's Motion for Summary Judgment in Bowles's case, that tooth was allegedly removed as a "precautionary" measure before she began chemotherapy. With a stronger warning of the risk posed by invasive dental procedures, it may be reasonably inferred that her dentist would have heeded that warning and adopted a "wait and see" approach rather than extracting the tooth.

In this respect, the Court finds that Dr. Skubitz's testimony concerning the benefits of strong warnings to avoid invasive dental procedures is relevant to Bowles's inadequate warning claim, and is admissible. However, the Court agrees that there is no evidence that a pretreatment dental screening would have made any difference in Bowles's [*53] case. Therefore, Dr. Skubitz's testimony on this topic is irrelevant and inadmissible.

The opposite is true with respect to Sheffer. NPC argues that Dr. Skubitz's testimony concerning warnings about avoiding invasive dental procedures is irrelevant because Sheffer's ONJ was not triggered by an invasive dental procedure. The Court agrees, NPC also argues that Dr. Skubitz's testimony about the benefits of pretreatment dental screening is irrelevant because Sheffer had regular dental care before beginning Zometa®. Sheffer notes, however, that she had documented signs of early periodontal disease before she began her Zometa® treatments, and was diagnosed with periodontal disease just a few months after she began her treatments. Harju Dep. at 41 (Ex. 6 to Vecchione Decl., Doc. #5479 in MDL-1760); Kroger Dep. at 39 (Ex. 4 to Vecchione Decl.). She argues that it can reasonably be inferred that if she had a pretreatment dental screening, she would have been diagnosed with periodontal disease at that time, and this would have altered her course of treatment. To this extent, the Court finds that Dr. Skubitz's testimony concerning the benefits of pretreatment dental screening is relevant to Sheffer's [*54] inadequate warning claim.

NPC also argues that Dr. Skubitz's opinion is not supported by reliable scientific evidence. It notes that Dr. Marx admits that "the jury is still out in terms of controlled data" concerning the benefits of pretreatment screening, and that the retrospective chart review on which Dr. Skubitz relies lacks a quantitative statistical analysis, Marx Dep. at 1366-67, 1381 (Ex. 7 to Doc. #30 in Case No. 3:12-cv-145).

The Court rejects these arguments. As Plaintiffs note, there are several studies cited in the record that support Dr. Skubitz's opinion, as do the guidelines issued by the American Association of Oral and Maxillofacial Surgeons. Ex. 12 to Doc. #40 in Case No. 3:12-cv-145. Even more significantly, David Epstein, NPC's own employee, admits that pretreatment screening is effective in reducing the risk of ONJ. Ex. 15 to Doc. #40 in Case No. 3:12-cv-145. The Court finds that Dr. Skubitz's opinion on this topic is relevant and reliable.

3. Drafting and Approval of Label Language

NPC notes that Dr. Skubitz has admitted that he is not an expert on the labeling of drugs. Skubitz Dep. at 159, 223-25; Ex. 3 to Doc. #30 in Case No. 3:12-cv-145. NPC seeks to exclude [*55] Dr. Skubitz's testimony "on the development of the Aredia® and Zometa® labeling language" and "NPC's participation and discussions with FDA regarding approval of the labels." Doc. #30 in Case No. 3:12-cv-145, at 10.

Citing Deutsch, 768 F. Supp.2d at 440, NPC argues that Dr. Skubitz should not be permitted to testify about whether the warnings complied with FDA regulations. The court in *Deutsch* agreed that Dr. Skubitz was not qualified to testify on this topic, but noted that it did not appear that plaintiffs intended to elicit any such testimony. It further held that Dr. Skubitz could offer his expert opinion "as to the adequacy of the labels from the perspective of [an] oncologist[] and prescribing physician[]." *Id.*

Dr. Skubitz plans to testify that the labels should have indicated that the risk of ONJ increases with cumulative doses of bisphosphonate drugs, and that ONJ occurs more frequently in patients treated with Zometa® than with Aredia®. NPC argues that these opinions are inadmissible because his hypothesis is based on literature that, for various reasons, is not scientifically reliable. The Court agrees with Plaintiffs, however, that Dr. Skubitz's opinions on this subject fall [*56] under the broad umbrella of testimony already deemed admissible by the MDL Court. It held that his testimony concerning "scientific and medical accuracy of the warnings given by Novartis is clearly more than unsupported speculation" and is admissible under *Daubert*. Ex. 2 to Doc. #40 in Case No. 3:12-cv-145. Under the law-of-the-case doctrine, this is not subject to reconsideration.

Finally, NPC argues that Dr. Skubitz's testimony concerning what should have been included on the labels is irrelevant to Plaintiffs' claims. It notes that the publications on which Dr. Skubitz relies were not available before Bowles developed ONJ. The MDL Court, however, has already held that there are genuine issues of material fact concerning what NPC knew about the risk of ONJ, and when. Ex. #1 to Dec. #47 in Case No. 3:12-cv-145. Moreover, although the warning labels were revised several times before Sheffer began Zometas® therapy, those label revisions did not address the specific risks that Dr. Skubitz opines should have been disclosed -- the increased risk of ONJ associated with cumulative doses of bisphosphonate drugs, and the increased risk of ONJ in patients treated with Zometa® instead of Aredia®. [*57] At this juncture, the Court cannot say that Dr. Skubitz's testimony is irrelevant to Plaintiffs' claims.

For these reasons, the Court finds that Dr. Skubitz may testify about what other information he believes should have been included on the drug labels.

4. Inclusion of Incidence Rate in Labels

Finally, NPC argues that Dr. Skubitz should not be allowed to testify that the Aredia® and Zometa® labels should have included information regarding an ONJ incidence rate of 5%. According to NPC, the only controlled studies show an incidence rate of just 1%. The Court agrees with Plaintiffs that Dr. Skubitz's testimony on what should have been included on the labels also falls under the broad umbrella of testimony already deemed admissible by the MDL Court. Accordingly, the Court will not revisit this issue since this is the law of the case.

B. Dr. James Vogel

Dr. James Vogel is a practicing oncologist and hematologist who regularly prescribes Aredia® and Zometa®, and has patients with bisphosphonate-induced ONJ. The MDL Court, in connection with the first "wave" of cases, already determined that Dr. Vogel is qualified to testify concerning general causation and the adequacy of the warning labels. [*58] *In re: Aredia and Zometa Products Liability Litigation*, No. 3:06-md-1760 (M.D. Tenn. Aug. 13, 2009) (Ex. 1 to Doc. #45 in Case No. 3:12-cv-145). It expressly declined to rule on the admissibility of his opinions concerning NPC's corporate conduct, the effect of the delay in transmitting adequate warnings, and the benefits of pretreatment dental screening. *Id.* NPC now seeks to exclude several of these categories of Dr. Vogel's expert witness testimony.

1. Corporate Conduct Related to Labeling

Dr. Vogel opines that NPC misrepresented causation evidence, referenced corticosteroids as potential risk factors for ONJ to misdirect the focus of attention away from the jaw area, minimized the incidence rate of ONJ, and failed to revise its labeling to indicate that ONJ occurs after fewer infusions of Zometa® than Aredia® and that reduced dosing levels decrease the incidence of ONJ. Vogel Report ¶ 62 (Ex. 1 to Doc. #31 in Case No. 3:12-cv-145).

NPC seeks to exclude this testimony on three grounds: (1) it is not based on any scientific or technical expertise and, therefore, is not an appropriate topic for expert testimony; (2) Dr. Vogel, who admits that he is not an expert on prescription drug labeling [*59] and has never worked for a pharmaceutical company, is not qualified to render an opinion on this subject; and (3) it is unreliable, speculative, and based on a limited review of corporate documents.

The Court rejects each of these arguments. Dr. Vogel's scientific knowledge and medical expertise will help the trier of fact to understand the evidence and to determine whether NPC adequately warned of the risk. *See* Deutsch, 768 F. Supp.2d at 443 ("It may not be apparent to a layperson what type of information a doctor expects to receive from the company advertising a drug and what information they are expected to and are able to ascertain on their own. Furthermore, it may not be apparent to a layperson why including some risk factors and not others are misleading to a prescribing doctor.") It is, therefore, a proper topic of expert testimony. Fed. R. Evid. 702(a).

As with Dr. Skubitz, the fact that Dr. Vogel is not an expert on prescription drug labeling does not disqualify him from testifying, from a physician's point of view, that certain labels are false or misleading or lack critical information. *See* Deutsch, 768 F. Supp.2d at 440-41. He will not, however, be permitted to testify about [*60] NPC's intent, motive, or state of mind since this is not an appropriate subject of expert witness testimony. *Id.* at 442.

NPC also argues that Dr. Vogel's criticisms are based on documents cherry-picked by Plaintiffs' counsel, and are based on insufficient facts and data. These objections, however, go to the weight to be given Dr. Vogel's testimony, not its admissibility.

2. Pretreatment Dental Screening

NPC also asks the Court to exclude Dr. Vogel's opinion that preventative dental screening done prior to bisphosphonate treatment reduces the risk of ONJ. Vogel Report at ¶61. It first argues that, because he is not a dentist or oral surgeon, he is not qualified to issue such an opinion. The Court disagrees, As the court held in *Deutsch*, "Dr. Vogel's extensive experience as an oncologist and hematologist including treating patients with bisphosphonate therapy provides a reliable basis for his opinions on the benefits of preventative measures such as pretreatment dental screening," 768 F. Supp.2d at 437.

NPC further argues that Dr. Vogel's opinion is not based on sufficient, reliable facts or data. NPC notes that the LaVerde article[2] did not analyze the benefits of pretreatment screening, [*61] but rather dental monitoring of patients who were already on bisphosphonates. Dr. Vogel, however, did not base his opinion on that article, but on case reports. 4/2/09 Vogel Dep. at 275 (Ex. 3 to Doc. #31 in Case No. 3:12-cv-145). Moreover, as previously noted, there is significant medical literature pointing to the benefits of pretreatment screening, and one of NPC's own employees has admitted that screening is effective in reducing the risk of ONJ. Ex. 15 to Doc. #40 in Case No. 3:12-cv-145. The Court finds that Dr. Vogel's opinion on this issue is admissible. *See* Deutsch, 768 F. Supp.2d at 438 (finding that Dr. Vogel's opinion on this issue satisfies the *Daubert* standard). NPC is free to challenge the bases for his opinion on cross-examination.

> 2 LaVerde, *Osteonecrosis of the Jaw (ONJ) in Cancer Patients Treated With Bisphosphonates: How the Knowledge of a Phenomenon Can Change Its Evolution*, Support Care Cancer (2008) (Ex. 7 to Doc. #31 in Case No. 3:12-cv-145).

NPC also argues, in a footnote, that evidence of the benefits of pretreatment dental screening is irrelevant to the cases at issue. With respect to Sheffer, the Court rejects this argument for the reasons previously [*62] stated in Section III(A)(2). However, with respect to Bowies, since there is no evidence that pretreatment dental screening would have made any difference, the Court agrees that Dr. Vogel's testimony is irrelevant and inadmissible.

3. Incidence Rates of ONJ

Dr. Vogel opines that the incidence rate of ONJ among patients taking Zometa® is "generally five percent or above." Vogel Report ¶ 47. NPC maintains that this opinion should be excluded because it is based on insufficient data. According to NPC, the articles on which Dr. Vogel relies have no uniform diagnostic criteria for ONJ, and he failed to consider data from later, randomized, double-blind controlled studies showing that the incidence rate is closer to one percent. NPC also argues that he selectively relied on his own experience with patients.

In his report, however, Dr. Vogel cites to numerous publications that support his opinion concerning the five percent incidence rate. *Id.* at ¶49. In the Court's view, NPC's objections go to the weight to be given to Dr. Vogel's testimony, not to its admissibility. He may, therefore, testify concerning the five percent incidence rate.

4. Dose and Duration

NPC also seeks to exclude Dr. Vogel's [*63] opinion that a reduced dosing schedule would be just as effective and less risky, and that NPC should have disseminated this information to the medical community. NPC maintains that Dr. Vogel's opinion is based on the Corso study, which NPC again argues is scientifically unreliable. For the reasons stated above in Section III(A)(1), the Court rejects this argument.

NPC further argues that the Court should exclude Dr. Vogel's opinion that NPC improperly failed to disseminate information to health care providers about re-

duced dosing schedules. Citing *Brodie v. Novartis Pharmaceuticals Corp.*, No. 4-10CV00138, 2012 U.S. Dist. LEXIS 189186, *3-4 (E.D. Mo. Jan. 20, 2012) (Ex. 5 to Doc. #31 in Case No. 3:12-cv-145), NPC argues that this is not a topic within Dr. Vogel's area of expertise.

Regardless of whether the Court finds that Dr. Vogel is qualified to testify on this topic, Plaintiffs have failed to show how his testimony is relevant to their claims. NPC notes that both Plaintiffs ceased their bisphosphonate drug therapy before the studies concerning reduced dosing were published. Again, Plaintiffs completely fail to respond to this argument, Because Plaintiffs have failed to show that Dr. Vogel's testimony on this [*64] topic is relevant to their claims, it is inadmissible.

5. Mechanism of Action

Finally, NPC seeks to exclude Dr. Vogel's opinion that bisphosphonates are more likely to accumulate in the jaw than in other bones due to higher remodeling rates and uptake. Rebuttal Report ¶16 (Ex. 16 to Doc. #31 in Case No. 3:12-cv-145). Dr. Vogel admits that he is not an expert on bone physiology. *Id.* NPC notes that, based on this admission, one court found that Dr. Vogel was not qualified to opine on how bisphosphonates affect bone. *Brodie*, at 2-3.

In admitting Dr. Vogel's testimony concerning general causation, however, the MDL Court has already impliedly held that Dr. Vogel is qualified to testify on this topic. Moreover, "he is not proffering this opinion as the definitive mechanism, but rather for the proposition that it is a plausible mechanism that has been identified based on his professional understanding of the relevant literature." *Deutsch*, 768 F. Supp.2d at 439. The Court will, therefore, allow him to testify concerning the mechanism of action.

C. Dr. Suzanne Parisian

Dr. Suzanne Parisian is a board-certified pathologist who was previously employed by the FDA. She is now a regulatory consultant, [*65] and was retained by Plaintiffs as an expert witness to testify about NPC's compliance with FDA regulations in connection with the development and marketing of Aredia® and Zometa®.

1. Qualifications

NPC argues that Dr. Parisian is not qualified to offer opinions concerning compliance with FDA regulations because her previous employment with the FDA was in the area of medical devices, not prescription drugs, and she has never worked for a pharmaceutical company. This argument has been consistently rejected by every transferor court to address it. *See, e.g., Brown v. Novartis Pharms. Co.*, No. 7:08-cv-130, Mem. and Recommendation, 2012 U.S. Dist. LEXIS 189189, *8-9 (E.D.N.C. Jan. 9, 2012) (Ex. 2 to Doc. #32 in Case No. 3:12-cv-145); *Winter v. Novartis Pharm. Co.*, No. 06-4049-CV-C, Order, at 5-6 (W.D. Mo. March 8, 2012) (Ex. 8 to Doc. #44 in Case No. 3:12-cv-145).[3] This Court also finds that Dr. Parisian "is qualified to testify with regard to the FDA in general and the regulatory requirements relating to the development, testing, marketing, and post-market surveillance of prescription drugs." *Deutsch*, 768 F. Supp.2d at 464.

3 Dr. Parisian's testimony was excluded in its entirety in *Hogan v. Novartis Pharmaceuticals Corp.*, No. 06 Civ. 260, 2011 U.S. Dist. LEXIS 43800, 2011 WL 1533467, at *2 (E.D.N.Y. Apr. 24, 2011) [*66] . The court found her testimony on regulatory matters to be irrelevant because the plaintiff's claims, grounded solely in state law, made no reference to FDA regulations. This case is factually distinguishable on that basis.

NPC further argues that Dr. Parisian's testimony must be excluded because she acts as a "superlawyer," usurping the jury's function of deciding the facts, and offering impermissible legal conclusions about whether NPC acted in compliance with FDA regulations. She admitted at her deposition that the FDA has not made a written determination that NPC violated any regulations in connection with its development, marketing, labeling and monitoring of Aredia® and Zometa®, 4/17/09 Parisian Dep. at 469 (Ex. 14 to Doc. #32 in Case No. 3:12-cv-145).

The Court agrees that it is not the function of an expert witness to offer legal conclusions, and Dr. Parisian will not be permitted to do so. Nevertheless, based on her experience, Dr. Parisian is entitled to offer testimony about what the FDA regulations require of drug manufacturers. *See Georges v. Novartis Pharm. Corp.*, Case No. CV06-5207, Order at 10-11 (C.D. Cal. [*67] Nov. 2, 2012) (Ex. 13 to Doc. #44 in Case No. 3:12-cv-145).

2. Qualification to Testify about Regulatory Causation

NPC next urges the Court to exclude Dr. Parisian's testimony concerning "regulatory causation," arguing that she is not qualified to offer her opinion on this topic. Plaintiffs do not intend to have her testify about medical causation, *i.e.*, whether the use of bisphosphonate drugs causes ONJ. Instead, they want to elicit her testimony about a "causal association" between the two. At a *Daubert* hearing in *Talley v. Novartis Pharmaceuticals Corp.*, No. 3:08-cv-361, Tr. at 124 (W.D.N.C. June 20, 2011) (Ex. 16 to Doc. #32 in Case No. 3:12-cv-145), Dr. Parisian explained that "regulatory causation" is distinguishable from "medical causation," and concerns "the

type of information that physicians and dentists need to know in order to care for their patients."

Several transferor courts have rejected this alleged distinction as confusing and misleading. They have not allowed Dr. Parisian to testify at all with respect to causation, finding her unqualified to offer an opinion related to the cause or diagnosis of ONJ. *See Brown*, Mem. and Recommendation, at 11-12; *Georges*, Order at 12. [*68] In *Deutsch*, the court found that Dr. Parisian's opinion -- that NPC acted improperly in disregarding certain case reports from the clinical trials -- was necessarily based on her opinion that the case reports involved bisphosphonate-induced ONJ. Because Dr. Parisian was not qualified to diagnose bisphosphonate-induced ONJ, neither was she qualified to offer an opinion concerning the propriety of NPC's actions. 768 F. Supp.2d at 469. The Court finds this reasoning persuasive. Accordingly, Dr. Parisian will not be permitted to testify about "regulatory causation" or a "causal association" between bisphosphonate drugs and ONJ.

3. Qualification to Testify about Adequacy of Warning Labels

NPC also argues that Dr. Parisian is not qualified to testify about the adequacy of NPC's warning labels for Aredia® and Zometa®, and that she lacks a basis for her opinion on this topic. It notes that she does not profess to be an expert on these drugs, and has never prescribed them or weighed their risks and benefits. However, as the court noted in *Brown*, Dr. Parisian has extensive experience in drafting and reviewing product labels, and almost all of the courts that have addressed this issue have considered [*69] her to be well qualified to testify on this topic. *Brown*, Mem. and Recommendation, at 12-13.

NPC further notes that Dr. Parisian has not drafted any alternative labeling that would have been more appropriate. Some courts have excluded expert witness testimony concerning the adequacy of warnings where the expert failed to propose any suitable alternative. *See Bourelle v. Crown Equip. Corp.*, 220 F.3d 532, 539 (7th Cir. 2000); *Jaurequi v. Carter Mfg. Co., Inc.*, 173 F.3d 1076, 1084 (8th Cir. 1999). Even though Dr. Parisian has not actually drafted an alternate warning for Aredia® and Zometa®, she did at least consider alternate language, and allegedly testified that she preferred the text originally proposed by the FDA. *See Georges*, Order at 14. At least two other transferor courts have held that this distinguishes her testimony from the expert witness testimony in *Bourelle* and *Jaurequi*. *Id.; Brown*, Mem. and Recommendation, at 14. This Court agrees that Dr. Parisian may testify about the adequacy of NPC's warning labels for Aredia® and Zometat®.

4. Other Testimony

NPC also asks the Court to exclude Dr. Parisian's testimony concerning medical causation, corporate intent and motive, compliance [*70] with non-FDA industry standards, monitoring of clinical trials, and ghostwriting of publications. Plaintiffs, however, indicate that they do not plan to elicit any such testimony. Therefore, the Court need not address these issues at this time.

Finally, NPC summarily asks the Court to exclude, as irrelevant, confusing and unfairly prejudicial, Dr. Parisian's: (1) criticism of the FDA and the pharmaceutical industry unless it is related to Aredia®, Zometa®, and ONJ; (2) testimony regarding drugs other than Aredia® and Zometa® and injuries other than ONJ; and (3) events that occurred after Plaintiffs developed ONJ. The Court agrees with Plaintiffs that NPC has failed to provide sufficient detail about any of this proposed testimony to allow the Court to rule on its admissibility at this time. The Court therefore overrules NPC's motion without prejudice to renewing the objections at trial, where they can be considered in the appropriate context.

D. Professor Wayne Ray

Wayne Ray is an epidemiologist, and Professor of Preventative Medicine and Director of the Division of Pharmacoepidemiology at Vanderbilt University School of Medicine. He has published numerous articles, most concerning the [*71] adverse and beneficial effects of medications. He was hired by Plaintiffs to address the question of general causation, *i.e.*, whether Aredia® and Zometa® cause ONJ. He admits that there are no controlled studies that establish a statistically significant association between the use of bisphosphonate drugs and ONJ. 2/21/09 Ray Dep. at 425-26 (Ex.1 to Doc. #33 in Case No. 3:cv-145). His opinion on general causation is therefore based on a meta-analysis, combining information he extracted from several observational studies.

In his report, he concludes that IV bisphosphonate drugs cause ONJ, and the longer the drugs are used, the greater the risk of developing such. He further opines that because there was no other credible explanation, NPC should have known of the causal connection as early as 2003. Ex. 2 to Doc. #33 in Case No. 3:12-cv-145. NPC seeks to exclude Professor Ray's expert witness testimony on several grounds.

1. Qualifications to Perform Meta-analysis

According to NPC, Professor Ray is not qualified to perform a meta-analysis because he has never published a meta-analysis in a peer-reviewed journal, and lacks the requisite medical expertise to understand other possible causes [*72] of ONJ. NPC further notes that Professor Ray failed to consult with any other doctors or clinicians in reaching his conclusions.

These same arguments have been repeatedly rejected by other transferor courts. *See, e.g.,* Deutsch, 768 F. Supp.2d at 454-55; *Bessemer v. Novartis Pharm. Corp.*, No. MID-L-1835-08, Mem. of Decision, at 6-8 (N.J. Super. Ct., April 30, 2010) (Ex. 2 to Dec. #46 in Case No, 3:12-cv-145). As the court noted in *Deutsch*, Professor Ray may not have published a meta-analysis, but he has used this method of analysis on numerous occasions and has significant experience as a pharmacoepidemiologist in analyzing research studies on the adverse effects of medication. Moreover, although he usually collaborates with others when conducting *original* research, that is not a standard practice when analyzing studies conducted by others. 768 F. Supp.2d at 455. Based on the reasoning in *Deutsch*, this Court also finds that Professor Ray is qualified to perform a meta-analysis.

2. Challenges to Methodology

NPC next challenges the reliability of several methodologies used by Professor Ray, particularly in connection with Tables 5 and 6 of his Revised Report, Ex. 11 to Doc. #33 in Case No. [*73] 3:12-cv-145.

In Table 5, Professor Ray compared the incidence rate of ONJ in IV bisphosphonate users who took the drugs for less than three months with those who took the drugs for more than three months. NPC argues that there is no scientific basis for this cut point. Professor Ray cites, however, to an article discussing guidelines for dental procedures for patients beginning IV bisphosphonate therapy. That article states that patients who have received less than three months of bisphosphonate therapy may be treated the same as those who have had no therapy. 2/20/09 Ray Dep. at 144-45 (Ex. 7 to Doc. #33 in Case No. 3:12-cv-145). Moreover, as Professor Ray explained in his report, this time period "is long enough to provide sufficient person-time to estimate a relative risk denominator, but short enough to limit the chronic effects of bisphosphonate use on risk of osteonecrosis of the jaw." Revised Report at 23. The Court finds that Professor Ray has adequately justified the three-month cut point. *See* Deutsch, 768 F. Supp.2d at 455-56.

NPC also argues that, because Professor Ray subjectively excluded 12 of the 26 observational studies he collected, and specifically excluded randomized, [*74] controlled studies, his conclusions fail to adequately account for confounding causes such as tooth extractions, thereby overstating the risk of developing ONJ from Aredia® or Zometa®. Ray explained, however, that he could determine the relative risk without controlling for these alternate factors, because there is no evidence that these factors cause ONJ in the absence of bisphosphonate use, Revised Report, at 30-33. The Court finds that Professor Ray has satisfied his burden under *Daubert*. Any objections concerning his failure to adequately account for confounding causes goes to the weight of his testimony, not its admissibility. *See* Deutsch, 768 F. Supp.2d at 456-57.

As shown in Table 6 of his Revised Report, Professor Ray also opines that Zometa® poses a higher risk than Aredia®. NPC argues that this opinion is flawed. Although Ray concludes that duration of therapy is associated with increased risk, Table 6 fails to account for such. He simply assumes that, since Aredia® has been on the market longer than Zometa®, patients taking Zometa® are likely to have a shorter duration of therapy. He fails to point to anything to support this assumption, and he admitted at his deposition [*75] that if his assumption is wrong, then the analysis reflected in Table 6 would be inaccurate. 2/20/09 Ray Dep. at 313.

On this basis, at least three other transferor courts have excluded his opinion that Zometa® poses a higher risk than Aredia®. *See* Deutsch, 768 F. Supp. 2d at 458; *Mahaney v. Novartis Pharm. Corp.*, No. 1:06-cv-35, Mem. Op. & Order, at 21-22 (W.D. Ky. Sept. 9, 2011) (Ex. 15 to Doc, #33 in Case No. 3:12-cv-145); *Winter*, Order at 15-16. This Court finds the reasoning set forth in those opinions to be persuasive. Accordingly, the Court excludes Professor Ray's testimony on this topic.

3. Admissibility of Other Causation-Related Opinions

NPC next argues that because Professor Ray's meta-analysis is flawed and inadmissible, his derivative causation opinions, including his Bradford-Hill analysis, must be excluded as well. A Bradford-Hill analysis is a set of criteria used to evaluate "a purported causal link between a chemical agent and a particular disease." *Castellow v. Chevron USA*, 97 F. Supp.2d 780, 786 (S.D. Texas 2000). Unless there is a statistically significant association between the drug and the disease, the Bradford-Hill analysis to determine causation is inapplicable. [*76] *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 569 (W.D. Pa. 2003). NPC argues that because the alleged association is based on the flawed meta-analysis, the Bradford-Hill analysis is unreliable. Because the Court has found that the underlying meta-analysis is reliable and admissible, the Court rejects this argument.

NPC also argues that Professor Ray's causation opinions should be excluded because they are based, in part, on anecdotal "adverse event" case reports that he admittedly never reviewed, 2/27/10 Ray Dep. at 197 (Ex. 8 to Doc. #33 in Case No. 3:12-cv-145). NPC maintains that such case reports are flawed in that they "reflect only reported data, not scientific methodology." *Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194, 1199 (11th Cir. 2002). Professor Ray's reliance on these case reports does not require exclusion of his testimony. As one court

noted, "Professor Ray is not relying on the truth of what is contained in these reports, but rather the significance of the increase in the reports absent any alternative explanation." *Deutsch*, 768 F. Supp.2d at 458.

NPC next urges the Court to exclude Professor Ray's testimony that it is biologically plausible that IV bisphosphonate [*77] drugs increase the risk of ONJ. NPC argues that he lacks the medical expertise to address this issue. It also notes that he admitted that the precise mechanism by which bisphosphonate drugs cause ONJ is not yet understood. Revised Report at 38. Professor Ray offers this opinion, however, not as a medical expert, but rather in the context of his epidemiologic assessment of causation. Because "biological plausibility is directly linked to the Bradford-Hill criterion," *Winter*, Order at 18, and Professor Ray is qualified to perform that causation analysis, his opinion on biological plausibility is admissible. Moreover, his hypothesis has strong support in medical literature. *See* *Deutsch*, 768 F. Supp.2d at 459-60.

NPC also seeks to exclude Professor Ray's opinion that NPC should have known in 2003 that Aredia® and Zometa® cause ONJ. It argues that, at that time, there were no published studies showing a causal relationship. The one publication that explored the topic, written by Dr. Robert Marx, acknowledged that "no definite cause and effect relationship has yet been established."[4] NPC notes that at least two transferor courts have excluded Professor Ray's opinion on this topic. In *Hogan v. Novartis Pharm. Corp.*, No. 06 Civ. 0260, 2011 U.S. Dist. LEXIS 43800, 2011 WL 1533467, at *8 (E.D.N.Y. Apr. 24, 2011), [*78] the court characterized his testimony as more of a closing argument than a scientific conclusion. *See also Mahaney*, Op. at 23 (Ex. 15 to Doc. #33 in Case No. 3:12-cv-145).

4 Robert Marx, *Letters to the Editor: Pamidronate (Aredia) and Zoledronate (Zometa) Induced Avascular Necrosis of the Jaws: A Growing Epidemic*, 61 J. Oral Maxillofacial Surg. 1115, 1116. Ex. 18 to Doc. #33 in Case No. 3:12-cv-145.

Other courts, however, have allowed Professor Ray to testify that NPC could have known of the causal relationship in 2003. *See Winter*, Order at 18 ("the fact that causation has not been definitely established does not prevent experts from opining on the likelihood of causation"); *Deutsch*, 768 F. Supp.2d at 459 (finding that objections to Professor Ray's opinion on this topic went to weight rather than admissibility). Having already admitted Professor Ray's causation opinions based on case reports, and in light of the "liberal standard of admissibility," *Deutsch*, 768 F. Supp.2d at 459, the Court will permit Professor Ray to offer his opinion on when NPC could have concluded that there was a causal relationship between bisphosphonate drugs and ONJ. NPC may explore the allegedly flawed basis [*79] for his opinion on cross-examination.

Finally, NPC urges the Court to exclude Professor Ray's testimony that approximately 5% of IV bisphosphonate patients develop ONJ. He conceded that definitions of ONJ may vary, and that the actual rate could be lower. 2/27/10 Ray Dep. at 171. However, because Professor Ray's opinion concerning the incidence rate is supported by the medical literature, the Court finds that it is admissible. Again, NPC's objections go to the weight of the testimony rather than its admissibility.

In a similar vein, NPC seeks to exclude his testimony that ONJ is "not rare" among IV bisphosphonate patients. It argues that the word "rare" is too subjective. NPC notes that the courts in *Deutsch*, 768 F. Supp.2d at 459, and *Brodie*, Order at 4, excluded Professor Ray's testimony on this basis. The Court agrees that Professor Ray's characterization of the frequency with which ONJ occurs among these patients is inadmissible. He may testify as to the actual occurrence rate, but the jury will have to draw its own conclusion about how "rare" it is for bisphosphonate drug users to develop ONJ.

E. Dr. Robert Marx

Dr. Robert Marx is an oral and maxillofacia surgeon, and Chief of the [*80] Division of Oral and Maxillofacial Surgery at the University of Miami School of Medicine. He has conducted extensive research concerning the connection between the use of bisphosphonates and ONJ, and has published on this topic. He is also widely regarded as the individual primarily responsible for bringing this issue to the attention of the medical community.

NPC objects to Dr. Marx: (1) testifying that dental treatment measures prevent ONJ; (2) presenting his personal opinion that NPC engaged in bad faith conduct; (3) criticizing the clinical trials; (4) speculating that certain patients in the clinical trials had bisphosphonate-induced ONJ; (5) presenting a general causation opinion based on adverse event reports he has not reviewed; and (6) testifying about the biological mechanism by which bisphosphonates allegedly caused ONJ.

As Plaintiffs note, the MDL Court already denied a substantially identical motion seeking to exclude Dr. Marx's litigation-wide testimony in connection with a different "wave" of cases. Ex. 1 to Doc. #41 in Case No. 3:12-cv-145. NPC sought to exclude Dr. Marx's testimony on the causal connection between bisphosphonate drugs and ONJ; treatment and preventative [*81] measures for ONJ; alleged "bad faith" conduct by NPC; whether certain patients in the clinical trials for Aredia®

and Zometa® had bisphosphonate-induced ONJ; and criticisms of the clinical trials. *Id.* To the extent that the MDL Court ruled on these issues, this constitutes the law of the case. It found that Dr. Marx's testimony was admissible under *Daubert* but, for summary judgment purposes in those cases, it did not need to consider his opinions concerning: (1) NPC's alleged bad faith conduct; or (2) the clinical trials. It, therefore, did not rule on the admissibility of those particular opinions. *Id.*

1. Preventative Measures/Avoiding Invasive Procedures

NPC first argues that Dr. Marx's testimony concerning the benefits of obtaining a dental examination before taking Aredia® or Zometa®, and of avoiding oral surgery while taking these drugs, should be excluded. Marx Report ¶¶52-55 (Ex. 3 to Doc. #35 in Case No. 3:12-cv-145). NPC maintains that Dr. Marx has no scientifically reliable basis for his opinion that pretreatment examinations may help prevent ONJ. As Plaintiffs note, the MDL Court has already ruled that Dr. Marx's opinion on this issue is admissible. That ruling will not be [*82] revisited.

NPC also argues, however, that Dr. Marx's testimony, concerning the benefits of pretreatment screening and avoiding invasive dental procedures, should be excluded as irrelevant because it does not "fit" the facts of Plaintiffs' cases. As discussed above in Section III(A)(2), the Court finds that testimony concerning the benefits of pretreatment dental screening is relevant and admissible in the *Sheffer* case, but not the *Bowles* case, and testimony concerning avoiding invasive dental procedures is relevant and admissible in the *Bowles* case, but not the *Sheffer* case.

2. Bad Faith Conduct

NPC next argues that Dr. Marx's opinion, that NPC acted in bad faith in responding to the initial reports of ONJ in individuals treated with Aredia®, Marx Report ¶47, exceeds the scope of proper expert testimony. NPC notes that several transferor courts have excluded Dr. Marx's testimony on the question of NPC's corporate intent or state of mind. *See, e.g.,* Deutsch, 768 F. Supp.2d at 448; *Bessemer*, Mem. of Decision at 3.

Plaintiffs, however, do not intend to offer Dr. Marx's opinions on NPC's corporate intent or state of mind. Rather, they intend to elicit factual testimony about his personal dealings [*83] with NPC. After Dr. Marx approached NPC about a possible causal relationship between its bisphosphonate drugs and ONJ, NPC asked him to serve on an advisory board. Dr. Marx maintains that NPC ignored the recommendations of the advisory board. As the court held in *Deutsch*, although Dr. Marx may not offer a legal conclusion as to whether NPC acted in bad faith, he may testify "as a fact witness about his experiences working with Novartis and Novartis employees . . . It is for the jury to decide whether Dr. Marx's experiences imply that Novartis was acting in bad faith." 768 F. Supp.2d at 448.

3. Clinical Trial Criticisms

NPC also seeks to exclude Dr. Marx's testimony criticizing the methods used for conducting the clinical trials for Aredia® and Zometa®. NPC claims that Dr. Marx, who has never planned or managed any clinical trials relating to bisphosphonates, lacks the expertise to offer an expert opinion on this subject. It also claims that his criticisms are the product of hindsight bias and not based on a scientifically reliable methodology.

The Court agrees that Dr. Marx may comment about the fact that records of the clinical trials do not indicate that dental specialists were consulted, [*84] or that certain examinations were performed, but he cannot testify that this rendered the clinical trials defective in design. *See Mahaney*, Mem. Op. & Order, at 32 (holding that Dr. Marx "may not opine on the overall adequacy of the clinical trials or whether certain measures not a part of the trials were necessary for a full and thorough review"); Deutsch, 768 F. Supp.2d at 450 ("he is simply not qualified to opine on the adequacy of the clinical trials"); *Winter*, Order at 11 (excluding testimony on the overall adequacy of the clinical trials, but allowing "testimony regarding the lack of records . . . to the extent necessary for Dr. Marx to explain his opinion on whether the clinical trials included patients with [ONJ]"); Hogan, 2011 U.S. Dist. LEXIS 43800, 2011 WL 1533467, at *6 (same).

4. Occurrence of ONJ in Clinical Trial Patients

Next, NPC seeks to exclude Dr. Marx's post-hoc diagnosis that five patients in the clinical trials developed bisphosphonate-induced ONJ. Marx Rebuttal Report ¶¶14-19 (Ex. 4 to Doc. #35 in Case No. 3:12cv-145). It appears that this testimony falls under the umbrella of testimony deemed admissible by the MDL Court, but even if that is not true, this Court finds it to be admissible [*85] in any event.

NPC argues that Dr. Marx's opinion should be excluded because he has testified that exposed jawbone lasting longer than eight weeks is a key component of ONJ, 5/26/09 Marx Dep, at 1358 (Ex. 2 to Doc. #35 in Case No. 3:12-cv-145), and none of the patients at issue had exposed bone consistent with this definition. As the court noted in *Deutsch*, however, at the time the clinical trials were conducted, there was no working definition of bisphosphonate-induced ONJ.

> [B]ecause exposed bone was not yet known to be a relevant indicator of BRONJ, the records would not necessarily reflect the presence or absence of exposed bone. Given these limitations, it was reasonable for Dr. Marx not only to consider whether exposed bone was noted on the chart, but also to look to other circumstantial evidence of BRONJ. Given that exposed bone may have been present but not recorded, it would be unfair to permit Novartis' experts to use the absence of a reference to exposed bone to conclude BRONJ was not present, and then preclude the Plaintiffs from showing that the records contain other indicia of BRONJ that make it likely exposed bone was present, but not recorded.

Deutsch, 768 F. Supp.2d at 449.

Because [*86] this Court finds that reasoning persuasive, Dr. Marx will be permitted to offer his opinion about whether individuals in the clinical trials had bisphosphonate-induced ONJ.

5. General Causation Based on Adverse Event Reports

NPC also seeks to exclude Dr. Marx's opinion on general causation because it is based, in part, on adverse event reports, submitted to the FDA or to NPC that he has never read. NPC maintains that such anecdotal evidence does not constitute scientifically reliable proof of general causation. Again, the MDL Court has already ruled on this litigation-wide issue, and this Court will not disturb that ruling since it is the law of the case. Dr. Marx may testify about general causation. NPC is, of course, free to cross-examine him concerning the bases for his opinion.

6. Biological Mechanism

Finally, NPC argues that Dr. Marx should not be permitted to testify about the biological mechanism by which bisphosphonate drugs allegedly cause ONJ. His hypothesis is that bisphosphonate drugs impair and kill osteoclasts, leading to oversuppression of bone remodeling, which occurs in the jaw at a higher rate. Marx Report ¶¶19-21. NPC argues that he is not qualified to testify on this [*87] topic, and that his opinion is unreliable because it is based on a study of fetal mouse cells instead of human cells.

The Court finds that, in admitting Dr. Marx's testimony on general causation, the MDL Court impliedly held that he could offer his opinion on this topic. *See Deutsch*, 768 F. Supp.2d at 438 ("Insofar as this was not among the topics explicitly excluded from the MDL court's opinion, the admissibility of Dr. Marx's opinion on this subject is the law of the case"); *Mahaney*, Mem. Op. & Order, at 33. In addition, this Court finds that Dr. Marx is qualified to offer his opinion on this topic, by virtue of his extensive knowledge, experience and research concerning the relationship between bisphosphonates and ONJ. Again, NPC is free to challenge the bases for his hypothesis on cross-examination, or to offer alternative theories.

IV. Conclusion

For the reasons set forth above, the Court SUSTAINS IN PART and OVERRULES IN PART each of the following:

> o Defendant's Motions to Exclude Testimony of Plaintiff's Expert Dr. Keith Skubitz (Doc. #30 in Case No. 3:12-cv-145, and Doc. #31 in Case No. 3:12-cv-238);
>
> o Defendant's Motions to Exclude Testimony of Plaintiff's Expert Dr. James Vogel [*88] (Doc. #31 in Case No. 3:12-cv-145, and Doc. #33 in Case No. 3:12-cv-238);
>
> o Defendant's Motions to Exclude Testimony of Plaintiff's Expert Dr. Suzanne Parisian (Doc. #32 in Case No. 3:12-cv-145, and Doc. #34 in Case No. 3:12-cv-238);
>
> o Defendant's Motions to Exclude Testimony of Plaintiff's Expert Professor Wayne Ray (Doc. #33 in Case No. 3:12-cv-145, and Doc. #35 in Case No. 3:12-cv-238); and
>
> o Defendant's Motion to Exclude Testimony of Plaintiff's Expert Dr. Robert Marx (Doc. #35 in Case No. 3:12-cv-145, and Dec. #36 in Case No. 3:12-cv-238).

More specifically, Plaintiffs' expert witness testimony is limited as follows:

> A. Dr. Keith Skubitz may not testify about alternative dosing schedules. He may testify about the benefits of pretreatment dental screening in the *Sheffer* case, but not in the *Bowles* case. He may testify about the benefits of avoiding invasive dental procedures in the *Bowles* case, but not in the *Sheffer* case. He may

also testify about the content of the drug labels, and the inclusion of the incidence rate on the drug labels.

B. Dr. James Vogel may not testify about NPC's motive, intent, or corporate state of mind, but may offer his opinion that the drug labels are false, [*89] misleading, or lack critical information. He may offer his opinion on the benefits of pretreatment dental screening in the *Sheffer* case, but not in the *Bowles* case. He may testify about the incidence rate of ONJ and the mechanism of action, but cannot testify about alternative dosing schedules.

C. Dr. Suzanne Parisian may testify about FDA regulatory requirements related to prescription drugs, and about the adequacy of the warning labels. She will not be permitted to testify about regulatory causation.

D. Professor Wayne Ray may testify about general causation. He may also testify that it is biologically plausible that IV bisphosphonate drugs increase the risk of ONJ, but may not testify that Zometa® poses a higher risk than Aredia®. He may also testify about when NPC should have known of the causal relationship. Although he may testify about the incidence rate of ONJ, he may not characterize ONJ as "not rare."

E. Dr. Robert Marx may testify about the benefits of pretreatment dental screening in the *Sheffer* case, but not in the *Bowles* case. He may testify about the benefits of avoiding invasive dental procedures in the *Bowles* case, but not in the *Sheffer* case. He may also testify about [*90] his experience on NPC's advisory board, but may not testify about corporate state of mind or intent. He may comment about records of the clinical trials, and may testify that certain individuals in the clinical trials developed ONJ. However, he may not offer an opinion about the overall adequacy of the clinical trials. He will be permitted to testify about general causation and the biological mechanism by which bisphosphonate drugs allegedly cause ONJ.

Date: September 20, 2013

/s/ Walter H. Rice

WALTER H. RICE

UNITED STATES DISTRICT JUDGE

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Exhibit M

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United States District Court, M.D. Florida,
Orlando Division.

Nancy GUENTHER and
Donald Guenther, Plaintiffs,
v.
NOVARTIS PHARMACEUTICALS
CORPORATION, Defendant.

No. 6:08–cv–456–Orl–31DAB.
|
March 28, 2013.

Attorneys and Law Firms

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ORDER

GREGORY A. PRESNELL, District Judge.

1 This matter comes before the Court after a hearing on the *Daubert* Motion to Exclude Certain Testimony of Plaintiffs' Expert Dr. Suzanne Parisian (Doc. 41) filed by the Defendant, Novartis Pharmaceuticals Corporation ("Novartis") and the response (Doc. 53) filed by the Plaintiffs.

A. Background

The instant products liability case involves Zometa, a drug manufactured by the Defendant. While undergoing treatment with Zometa, Plaintiff Nancy Guenther developed osteonecrosis of the jaw (henceforth, "ONJ"), a condition in which part of the jawbone essentially dies.

Parisian is an M.D. and a board-certified pathologist who worked for the FDA for four years in the area of regulation of medical devices. She is the founder of a regulatory and medical consulting firm that specializes in matters involving FDA regulations.

By way of the instant motion, Novartis first seeks to exclude all of Parisian's testimony on the grounds that the Plaintiffs have not established that her opinions are admissible under *Daubert* and Federal Rule of Evidence 702. Failing that, Novartis argues that Parisian should be precluded from offering testimony in the following areas: (a) corporate conduct; (b) legal conclusions; (c) regulatory compliance; (d) the issue of whether Novartis violated FDA rules or regulations with respect to its development, marketing, labeling, and monitoring or Zometa; (e) ONJ causation or diagnosis and so-called "regulatory causation"; (f) her opinions regarding labeling; (g) her opinions regarding the state of mind of Novartis or the FDA; (h) her opinion that Novartis failed to act "reasonably" or follow unspecified industry standards; (i) Novartis's alleged failure to adequately monitor the safety of clinical trial patients; (j) ghostwriting and company funding of publications; and (k) other "irrelevant, unfairly prejudicial, and confusing testimony."

II. Standards

In *Daubert v. Merrill Dow,* 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993), the Supreme Court admonished trial courts to fulfill a gatekeeping role in the presentation of expert testimony. Federal Rule of Evidence 702 ("Rule 702") provides that:

> If scientific ... knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

To guide district courts' assessments of the reliability of an expert's testimony, the Supreme Court has identified four factors that district courts should consider when assessing the reliability of an expert's testimony: (1) whether the expert's methodology has been tested or is capable of being tested; (2) whether the theory or technique used by the expert has been subjected to peer review and publication; (3) whether there is a known or potential error rate of the methodology; and (4) whether the technique has been generally accepted in the relevant scientific community. *See id.* at 593–94, 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469. At the same time, the Court has emphasized that these factors are not exhaustive and are intended to be applied in a "flexible" manner. *Kumho Tire Co., Ltd. v. Carmichael,* 526 U.S. 137, 141, 119 S.Ct. 1167, 143 L.Ed.2d 238 (1999).

***2** From the reference to "scientific knowledge" and the condition that it "will assist the trier of fact," the Supreme Court, in *Daubert,* interpreted Rule 702 to require that expert testimony on scientific matters have the following inter-connected attributes:

- that it be "scientific," having a "grounding in the methods and procedures of science";
- that it bear the hallmarks of "knowledge," which "connotes more than subjective belief or unsupported speculation"; and
- that it "assist the trier of fact" or "fit" a matter at issue, meaning that it expresses scientific knowledge as to the proposition for which it is offered.

Daubert, 509 U.S. 579, 592, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993). Expert testimony need not purport to reveal a known certainty, but it must be derived by the "scientific method," which requires that it be supported by appropriate validation based on what is known. *Id.*

III. Analysis

Although Novartis asserts in its motion that the entirety of Parisian's testimony should be excluded for failure to meet the *Daubert* standard, Doc. 41 at 1, it never squarely addresses the topic. Insofar as Novartis truly intended to question Parisian's qualifications to offer any testimony whatsoever, the Court finds that Parisian is generally qualified by virtue of, *inter alia,* her tenure with the FDA and her professional experience in the field of regulatory approval to offer opinions regarding the four broad subject areas described in her expert report (Doc. 41–19):(1) the role, process and functions of the FDA and the responsibilities of pharmaceutical drug sponsors; (2) Novartis' conduct regarding New Drug Application approvals and post-approval of Aredia and Zometa; (3) Novartis's pharmacovigilance efforts, investigation of ONJ and interactions with the FDA; and (4) Novartis's communication of ONJ risks to health care providers.

The majority of Novartis's motion is spent protesting allegedly objectionable testimony offered by Parisian in other trials or in depositions taken in other cases. At this juncture, the Court cannot determine whether the Plaintiffs will even seek to have Parisian repeat such testimony in this case, much less whether that testimony, in context, would be permitted.

The Plaintiffs have stipulated that, unless Novartis opens the door, Parisian will not be asked to testify regarding the following areas as to which Novartis has raised concerns: corporate state of mind (category "g" above"), industry standards (category "h"), monitoring of clinical trials (category "i"), and ghostwriting (category "j"). Thus, the motion is moot as to those categories.

Similarly, in regard to category "e", the Plaintiffs also stipulate that they will not ask Parisian to testify about medical causation. However, Plaintiffs' counsel stated that he may seek to have Parisian testify regarding what Novartis refers to as "regulatory causation". This line of inquiry involves 21 C.F.R. § 201.57, an FDA regulation having to do with drug labels, and which provides in pertinent part that

> ***3** the labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established.

21 C.F.R. § 201.57(c)(6)(i). The Defendant argues that allowing Parisian to testify regarding Novartis's compliance with that regulation is effectively the same as allowing her to testify regarding medical causation, allowing her to make an end run around her stipulation. (In other words, Novartis contends that to opine as to whether the label should have been revised, Parisian would need to discuss whether there was a causal association

between Zometa and ONJ, which is essentially the same as discussing whether there was a causal relationship between Zometa and ONJ.) Plaintiffs' counsel responds that "causal association" is an FDA term, rather than a medical term, and that Parisian as an FDA compliance expert should be permitted to testify in regard to that term. Aside from its origin, however, Plaintiffs' counsel offers nothing to meaningfully distinguish "causal association" from medical causation, at least in terms of the expertise required to analyze it. On this record, Parisian will not be permitted to offer opinions regarding any alleged "causal association" between ONJ and Zometa.

The Defendant's remaining points requires less discussion. Assuming that Parisian's assessment of Novartis's "corporate conduct" (category "a") has some relevance to the instant case, she will be permitted to testify to it, assuming that her opinions are otherwise properly supported. Obviously, Parisian will not be permitted to offer legal conclusions (category "b"), *see, e.g., Cook ex rel. Estate of Tessier v. Sheriff of Monroe County, Fla.*, 402 F.3d 1092, 1113 (11th Cir.2005), but an opinion is not objectionable just because it embraces an ultimate issue to be decided by the trier of fact, F.R.E. 704(a).

Finally, regulatory compliance (category "c"), alleged violations of FDA rules or regulations in regard to Zometa (category "d") and drug labeling (category "f") all appear to fall within Parisian's area of expertise. Subject to the usual requirements such as relevance and evidentiary support, Parisian will be permitted to offer expert testimony in these areas. And any other concerns Novartis has in regard to "irrelevant, unfairly prejudicial and confusing testimony" (category "k") can be addressed at trial or cured by way of cross-examination.

In consideration of the foregoing, it is hereby

ORDERED that the *Daubert* Motion to Exclude Certain Testimony of Plaintiffs' Expert Dr. Susan Parisian (Doc. 41) is **GRANTED IN PART and DENIED IN PART** as set forth above.

DONE and **ORDERED.**

All Citations

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Exhibit N

2012 WL 9064768
Only the Westlaw citation is currently available.
United States District Court,
C.D. California.

Adriann GEORGES
v.
NOVARTIS PHARMACEUTICALS CORP., et al.

No. CV 06–5207 SJO (VBKx).
|
Nov. 2, 2012.

Attorneys and Law Firms

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PROCEEDINGS (in chambers): ORDER DENYING DEFENDANT'S MOTION TO EXCLUDE CAUSATION TESTIMONY OF DR. ERIC SUNG [Docket No. 60]; **ORDER GRANTING IN PART AND DENYING IN PART DEFENDANT'S MOTION TO EXCLUDE TESTIMONY OF DR. SUZANNE PARISIAN** [Docket No. 58]; **ORDER GRANTING IN PART AND DENYING IN PART DEFENDANT'S MOTION TO EXCLUDE TESTIMONY OF DR. ROBERT MARX** [Docket No. 54]

The Honorable S. JAMES OTERO, District Judge.

***1** Victor Paul Cruz Courtroom Clerk

This matter comes before the Court on Defendant Novartis Pharmaceuticals Corporation's ("Defendant") three related motions: (1) Motion to Exclude Causation Testimony of Dr. Eric Sung ("Sung Motion"); (2) Motion to Exclude Testimony of Dr. Suzanne Parisian ("Parisian Motion"); and (3) Motion to Exclude Testimony of Dr. Robert Marx ("Marx Motion"). The Court found this matter suitable for disposition without oral argument and vacated the hearing set for October 9, 2012. *See* Fed.R.Civ.P. 78(b). For the following reasons, the Court grants in part and denies in part the various motions.

I. *FACTUAL AND PROCEDURAL HISTORY*

Defendant has concurrently filed a Motion for Summary Judgment (ECF No. 61), which provides a useful summary of facts. The following facts are not in material dispute. Defendant is a manufacturer of two drugs, Aredia and Zometa ("Treatment Drugs"), which are bisphosphonates used in the treatment of cancer that has metastasized to the bones. (Pl.'s Resp. to Def.'s Statement of Uncontroverted Facts and Conclusions of Law ("Defendant Facts") ¶ 1, ECF No. 95.) These drugs are prescribed to limit or prevent bone loss of various types associated with such metastases. (Def. Facts ¶ 6.) The Treatment Drugs remain on the market today, and physicians continue to prescribe them for the above treatment. (Def. Facts ¶¶ 7–8.)

Osteonecrosis of the Jaw ("ONJ") is an osseous pathology leading to the deterioration of bones in the jaw. (Def. Facts ¶ 9.) In December 2002, Defendant received a report that ONJ had developed in a patient using the Treatment Drugs. (Def. Facts ¶ 10.) Following further occurrences of ONJ in patients taking the Treatment Drugs, and a review of the available literature, In September 2003 Defendant voluntarily revised the "adverse Reactions" section of its labeling for both drugs to include a warning that some people using the drugs had reported cases of ONJ. (Def. Facts ¶ 20.) No published reports demonstrated an association between the specific use of Aredia and Zometa, and onset of ONJ (Def. Facts ¶ 10), but internal Defendant emails suggest that at least a few cases of ONJ arose during clinical testing of these drugs (Def. Facts ¶ 13).

Plaintiff was diagnosed with breast cancer in August 1989, and in August 1999 she was diagnosed with Stage IV metastatic breast cancer to her bones and lungs. (Pl's Statement of Uncontroverted Facts and Conclusions of Law ("Plaintiff Facts") ¶¶ 1, 2, ECF No. 96.) At the advice of her oncologist, Dr. Waisman, Plaintiff began taking Aredia, switching to Zometa in March 2002. (Pl. Facts ¶¶ 3–5.) During this time, Plaintiff also took several other drugs in the treatment regime, including medications for other related health issues. (Def. Facts ¶¶ 34–38.) Medical literature has listed several other medical treatments and conditions, including many that applied to Plaintiff concurrently with her use of the Treatment

Drugs, as risk factors in the development of ONJ. (Def. Facts ¶¶ 65–70.) However, Plaintiff asserts that there is a distinction between "regular" ONJ and bisphosphonate-related ONJ ("BRONJ"), which she was diagnosed with and which has no major risk factors apart from the use of bisphosphonates. (Def. Facts ¶¶ 65–70.)

***2** In March 2000, Plaintiff's oral surgeon, Dr. Radack, noticed an exposure in Plaintiff's lower right jaw. He extracted Plaintiff's tooth # 31 two months later and tooth # 30 in August 2001. (Pl. Facts ¶¶ 6–9.) Dr. Radack noticed further exposure on the lower left jaw in 2003, eventually removing Plaintiff's tooth # 18. (Pl. Facts ¶¶ 11–14.) Tooth # 19 later fell out on its own. (Def. Facts ¶ 54.) In 2004, after learning of a possible connection between use of the Treatment Drugs and ONJ, Dr. Radack informed Plaintiff of this possibility. (Decl. of John A. Girardi in Supp. of Pl.'s Opp'n to Summ. J. ("Plaintiff Exhibits"), Ex. 6, 56–58, ECF No. 99.)

Plaintiff continued treatment with Zometa until January 2005, when Dr. Waisman put Plaintiff's treatment on hold pending concerns that the Treatment Drugs were associated with ONJ. (Pl. Facts ¶¶ 5, 26–27; Pl.Ex. 16, 90:12–21.) Subsequently, Dr. Waisman referred Plaintiff to an expert at the University of California, Los Angeles ("UCLA") for further treatment specifically tailored to Plaintiff's ONJ. Plaintiff followed Dr. Radack's referral and began seeing Dr. Eric Sung for treatment in November 2006. (Def. Facts ¶ 56.) Dr. Sung diagnosed Plaintiff with ONJ in the right and left mandible and treated her accordingly, with the result that as of January 2011 Plaintiff has mostly healed, although some of her jaw remained exposed. (Def. Facts ¶¶ 56–59.)

Plaintiff filed the current case against Defendant in Los Angeles County Superior Court, from which Defendant removed the case to this Court on August 18, 2006. (Notice of Removal, ECF No. 1.) On October 12, 2006, the United States District Court for the Middle District of Tennessee ("MDL Court") approved transfer of the case to that district as part of a Multidistrict Litigation ("MDL") that handled discovery and resolution of preliminary issues for multiple cases against Defendant asserting bisphosp honate-ca used ONJ. (*See* Conditional Transfer Order, ECF No. 14.) The case was transferred back from MDL Court on July 28, 2011, for resolution of case-specific questions. (*See* Notice of Transfer/Remand and Reopening of Case, ECF No. 17.) Defendant filed all three of the present motions on September 11. (Marx Mot., ECF No. 54; Parisian Mot., ECF No. 58; Sung Mot., ECF No. 60) Plaintiff has filled oppositions to all three motions (Opp'n to Parisian Mot. ("Parisian Opposition"), ECF No. 92; Opp'n to Marx Mot. ("Marx Opposition"), ECF No. 97; Opp'n to Sung Mot. ("Sung Opposition"), ECF No. 102), and Defendant has replied in support of each motion (Reply in Supp. of Marx Mot. ("Marx Reply"), ECF No. 109; Reply in Supp. of Parisian Mot. ("Parisian Reply"), ECF No. 111; Reply in Supp. of Sung Mot. ("Sung Reply"), ECF No. 112).

II. *DISCUSSION*

The test for admissibility of expert witness testimony as laid out in Rule 702 allows a proposed expert witness to testify if "(a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles and methods; and (d) the expert has reliably applied the principles and methods to the facts of the case." Red. R. Evid. 702.

***3** The Supreme Court formed the basis for this standard in *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993), noting particularly that would-be expert witnesses must demonstrate a "reliable basis in the knowledge and experience of [their] discipline," *id.* at 592, where " 'knowledge' 'connotes more than subjective belief or unsupported speculation,' " *id.* at 599. The courts in general have a "gatekeeping responsibility" to ensure that these standards are met. *Id.* at 600. And parties wishing to introduce expert witnesses bear the burden of proof that such testimony is admissible. *Lust By & Through Lust v. Merrell Dow Pharms., Inc.*, 89 F.3d 594 (9th Cir.1996).

To be admissible, expert testimony, like all other forms of evidence, must be relevant. Fed.R.Evid. 401. The danger of unfair prejudice, confusion of the issues, misleading the jury, undue delay, waste of time, or needless presentation of cumulative evidence must not substantially outweigh the testimony's probative value. *See* Fed.R.Evid. 402; 403.

A. *Defendant's Motion to Exclude Dr. Sung's Testimony*

One of Plaintiff's primary expert witnesses is Dr. Sung, who is designated to testify, among other things, that the Treatment Drugs specifically caused Plaintiff's ONJ.

(Sung Mot. 1.) Defendant moves to exclude Dr. Sung's testimony as to specific causation on the basis that (1) Dr. Sung is unqualified to address the question of ONJ causation; and (2) Dr. Sung fails to utilize a reliable methodology to form his opinions. (Sung Mot. 1.) Defendant does not contest that Dr. Sung's testimony is based on sufficient facts or data (*see generally* Sung Mot.), and so the Court does not address the second factor in the Rule 702 test. Defendant also does not contest that Dr. Sung may testify regarding his diagnosis and treatment of Plaintiff.

1. *Dr. Sung's Qualifications*

Defendant first alleges that Dr. Sung simply does not have the requisite experience and knowledge to testify as to the causation of Plaintiff's ONJ. Defendant characterizes Dr. Sung's experience as limited to having treated approximately 25 individuals with ONJ and co-authored two studies involving ONJ-like lesions in rats. (Sung Mot. 9.) Defendant challenges the sufficiency of Dr. Sung's experience on the basis that (1) diagnosis and treatment of medical conditions does not qualify someone to determine the cause of such conditions; (2) causation research in rats does not equate to causation research in humans; and (3) Dr. Sung admits that he is not an expert in oncology, or in the functionality of any bisphosphonate drug, which makes him unqualified to testify as to their effect. (Sung Mot. 9–10.) Defendant further observes that "Dr. Sung is not a medical doctor, and he is not an oral/maxillofacial surgeon, pathologist, or specialist. He is a dentist." (Sung Reply 3.) Defendant then directs the Court to several cases excluding dentists from testifying as to causation. (Sung Reply 3–4.)

***4** Plaintiff responds by emphasizing Dr. Sung's experience in the field. As she demonstrates, Dr. Sung has focused on cancer in his dental work, treating and performing studies on head and neck cancer patients. (Sung Opp'n 8–10; Decl. of John A Girardi in Supp. of Sung Opp'n ("Plaintiff Sung Exhibits"), Ex. 5, Sung CV at 1–3, ECF No. 101.) Dr. Sung has also authored publications on cancer-related ONJ topics, including the incidence of ONJ as a complication of chemotherapy, certain risk factors for BRONJ, and managing BRONJ in patients; he has given numerous presentations on these topics as well as on the diagnosis and treatment of BRONJ. (Sung Opp'n 9–10; Sung CV 8–11.) And finally, he has consulted with oncologists specifically regarding dental treatment of cancer patients. (Pl. Sung Ex. 5.)

On the facts above, Dr. Sung is clearly qualified to testify. The Court is aware of no requirement that an expert testifying as to medical causation must have obtained a Doctorate of Medicine ("M.D."). Certainly a certified doctor is more likely to qualify as an appropriate expert, but *Daubert* requires only that an expert demonstrate a "reliable basis" in the relevant discipline, 509 U.S. at 592, and Dr. Sung in this circumstance has clearly demonstrated a broad-based knowledge of ONJ and its causes. Defendant's citation to caselaw disqualifying dentists from testifying as to specific causation is not helpful: in each of those cases, the court disqualified the dentists in question because plaintiffs had provided no indication that these dentists were experts on ONJ risk factors. *See generally In re Aredia & Zometa Prods. Liab. Litig. (Kyle/Mahaney)*, No. 06–495, slip op., 2010 WL 5071063 (M.D.Tenn. Dec. 7, 2010); *In re Aredia & Zometa Prods. Liab. Litig. (Baldwin/Winter)*, No. 06–496, slip op., 2010 WL 5071063 (M.D.Tenn. Dec. 7, 2010); *In Re Aredia & Zometa Prods. Liab. Litig. (Anderson)*, No. 08–1157, slip op. (M.D.Tenn. Aug. 13, 2009) ("Dr. Liang not only testified that he had no expertise in diagnosing [ONJ] ... but he also testified that he had no opinion as the cause of ... ONJ."). [1]

1 These cases might appropriately be used to exclude the causation testimony of Dr. Radack, but Plaintiff does not attempt here to qualify Dr. Radack as an expert witness on the question of specific causation. Dr. Sung was brought in specifically as an ONJ specialist to treat Plaintiff's injuries at the request of Plaintiff's oncologist, Dr. Waisman. This recognition from peers in the medical/dental community provides yet more evidence that Dr. Sung is qualified to discuss ONJ-related issues.

Defendant's other objections are similarly inapposite. Defendant is correct that diagnosis of medical conditions does not qualify someone to testify as to the causes of these conditions, but in this case Plaintiff has provided significant evidence suggesting independently that Dr. Sung is so qualified. And while causation in rats is certainly distinct from that in humans, Dr. Sung's involvement in studies examining risk factors for ONJ suggests at least that he is well versed in that area of medical research.

Defendant's own citation to supplemental authorities within the MDL only strengthens this conclusion. One such case suggests that an expert can be approved to

testify based on the strength of "his education and his experience treating [15 BRONJ] patients," even where the expert has not engaged in any significant academic work examining BRONJ risk factors. *Luttrell v. Novartis Pharm. Corp.*, No. 07–CV–3015–TOR, 2012 WL 4513109, at *9 (E.D.Wash. Oct.1, 2012). Dr. Sung has significantly more academic experience in the field of ONJ, and has treated 25 patients with ONJ, 10 more than the expert in *Luttrell.* Another case suggests that an expert's modesty as to his or her own expertise does not disqualify them as a witness. *Harvey v. Novartis Pharm. Corp.*, 2:06–CV–1140–VEH, 2012 WL 4713097, at *4 (N.D.Ala. Oct.4, 2012) ("Just as an individual cannot simply declare himself to be an expert, a person cannot simply declare himself not to be an expert."). Thus, Dr Sung's assertions that he is not an expert in oncology, and is just a dentist, need not disqualify him from testifying as an expert.

2. *Dr. Sung's Methodology*

***5** The larger part of Defendant's argument challenges the methodology Dr. Sung uses to draw his conclusion that the Treatment Drugs caused Plaintiff's ONJ. Specifically, Defendant argues that Dr. Sung's process for determining causation is insufficient because Dr. Sung did not employ "differential diagnosis." Differential diagnosis is defined as "the determination of which of two or more diseases with similar symptoms is the one from which the patient is suffering, by a systematic comparison and contrasting of the clinical findings." Stedman's Medical Dictionary 474 (28th Ed.2006). In the context of the court system, this meaning has been amended slightly: "courts have used the term in a more general sense to describe the process by which *causes* of the patient's *condition* are identified. *Clausen v. M/V NEW CARISSA,* 339 F.3d 1049, 1057 n. 4 (9th Cir.2003).

Defendant provides significant evidence in support of its assertion that Dr. Sung did not conduct differential diagnosis. Most notably, Dr. Sung has testified explicitly that he did not conduct differential diagnosis with respect to Plaintiff's condition:

> Q. Did you perform any type of differential diagnosis with regards to Ms. Georges' osteonecrosis of the jaw?
>
> A. No.6
>
> Q. Did you consider any other risk factor for ONJ that Ms. Georges has other than bisphosphonate use?
>
> A. No.
>
> Q. And it's your opinion that Ms. Georges has osteonecrosis of the jaw from—due to her Aredia and/or Zometa use. Correct?
>
> A. Correct.

(Sung Mot. 13–14; Def. Ex. 76 ("Sung Dep."), 172–73.) Defendant further observes that Dr. Sung "did not look at the history" of Plaintiff's condition, instead focusing on "what we do from here" (Sung Dep. 175), and that he has admitted to not considering the possibility that Plaintiff's metastatic cancer spread to her jaw, causing her ONJ (Sung Dep. 70, 185–86).

Plaintiff argues in return that there is a clear scientific basis for Dr. Sung's conclusions. She cites first to Dr. Sung's expert report, prepared for this litigation, in which he declares the following:

> At the time of my initial examination of the patient in which her history was obtained from her and her husband in detail, and my subsequent research, it was my opinion the patient has osteonecrosis of the jaw (ONJ) resulting from the infusion of *Aredia* and *Zometa* medications, and not resulting from metastatic cancer, or in other words, the ONJ was not a manifestation of spreading breast cancer.... All these opinions are based upon my personal observations and the results of a multiplicity of laboratory studies at UCLA as well as those secured by [prior] health providers.

(Pl.Ex. 6, at 2.) Plaintiff further argues, contrary to Defendant, that Dr. Sung did in fact perform differential diagnosis here. Most notably, when asked about performing differential diagnosis, Dr. Sung testified that Plaintiff's ONJ "was obviously ONJ secondary to bisphosphonate, and given such, the other differential diagnosis may have been around my head. I think they were fairly quickly dismissed, given what I saw." (Sung Dep. 233.) In short, Plaintiff argues that Dr. Sung "considered the usual array of alleged causes based on his

clinical experience and reading of the literature, and ruled them out." (Sung Opp'n 13.)

***6** Both parties agree that if Dr. Sung's analysis is underpinned by differential diagnosis, it should be admitted, and the Court concurs. The Ninth Circuit has explicitly held that differential diagnosis is a "reliable methodology" for determining causation. *Clausen,* 339 F.3d at 1058. It has also declined to overturn district courts' holdings that certain expert testimony is inadmissible where the expert failed to conduct a proper differential diagnosis. *Morin v. United States,* 244 F. App'x 142, 143 (9th Cir.2007); *Whisnant v. United States,* 274 F. App'x 536, 537 (9th Cir.2008). In short, differential diagnosis is a significant factor to consider in evaluating the sufficiency of an expert's process—and at the least, expert testimony based in part on a properly conducted differential diagnosis is likely to be admissible.

In this case, Dr. Sung did not conduct an explicit, formal differential diagnosis of Plaintiff's condition when he first saw her. In addition to having testified to that fact, Dr. Sung admits that he did not initially consider the possibility that Plaintiff's ONJ might have resulted from her metastatic cancer, because "in his mind" it was clearly bisphosphonate-related ONJ. Defendant's citation to cases within this MDL provide a basis to exclude Dr. Sung's testimony. *See Luttrell,* 2012 WL 4513109, at *10–11 (excluding testimony from an expert testifier because he did not provide evidence that he had assessed and dismissed other risk factors); *Harvey,* 2012 WL 4713097 at *6 ("[Expert's] failure to give a reasonable explanation for concluding that bisphosphonate drug use rather than osteomyelitis caused [plaintiff's] injury renders his differential diagnosis not sufficiently reliable."). As in the experts in *Luttrell* and *Harvey,* Dr. Sung here does not provide significant testimony in support of his differential diagnosis, and has admitted to having not conducted a formal differential diagnosis with respect to Plaintiff's ONJ.

This does not complete the Court's analysis, however: the question mandated to this Court by *Daubert* is not whether Dr. Sung conducted a formal differential diagnosis, but whether his procedures were, taken as a whole, fundamentally flawed in some way. The Ninth Circuit, per above, puts great value in a properly conducted differential diagnosis, but it "has never explicitly rejected or validated expert causation testimony based on a [formal] differential diagnosis ... [while recognizing] its use as **a** reliable methodology." *Clausen,* 339 F.3d at 1058 (emphasis added). There is no indication that differential diagnosis should replace the *Daubert* standard in the context of medical causation testimony, and this Court declines to change this standard here.

Further, the Court does not agree with Defendant that Dr. Sung failed entirely to conduct any sort of differential diagnosis. The definition as acknowledged by the Ninth Circuit contemplates a more holistic set of activities:

> ***7** A reliable differential diagnosis typically, though not invariably, is performed after physical examinations, the taking of medical histories, and the review of clinical tests, including laboratory tests, and generally is accomplished by determining the possible causes for the patient's symptoms and then eliminating each of these potential causes until reaching one that cannot be ruled out **or determining which of those that cannot be excluded is the most likely.**

Clausen, 339 F.3d at 1057 (quoting *Westberry v. Gislaved Gummi AB,* 178 F.3d 257, 262 (4th Cir.1999) (citation and internal quotation omitted). Here, although Dr. Sung admits that he did not conduct a **formal** differential diagnosis at the start, there is strong indication that he conducted an **informal** differential diagnosis, and later confirmed his initial suspicions through his clinical work and other tests. As Dr. Sung has testified, when Plaintiff first came in for treatment he considered some non-bisphosphonate risk factors, but dismissed them "fairly quickly" based on what he saw of Plaintiff's condition. (Sung Dep. 233.) This alone suggests that Dr. Sung made at least some consideration of causation. More tellingly, Dr. Sung's expert report indicates that his diagnosis, which included a finding as to causation, was based on Plaintiff's medical history, a physical examination, laboratory tests, and his knowledge of ONJ and BRONJ. This squares quite well with the process anticipated in *Clausen,* and particularly so when considering that the process anticipated in *Clausen* does not require that an expert eliminate all other possible causes of BRONJ so long as he can determine which cause is the most likely. Thus, even were differential diagnosis required, Dr. Sung

has demonstrated conformity with the requirements laid out by the Ninth Circuit.

Based on the sum total of the evidence, and considered in a light favorable to Plaintiff, the Court finds Dr. Sung's testimony to be admissible. The Ninth Circuit has allowed district courts, in their discretion, to exclude expert testimony where the experts "failed to account for possible alternate causes," *see Whisnant,* 274 Fed. App'x at 537, but it has not held that district courts must exclude helpful expert testimony merely for failing to conduct a formal differential diagnosis. Defendant has provided substantial evidence that Dr. Sung's process may have been incomplete in different ways, and it is free to challenge Dr. Sung's conclusions on the stand accordingly; but challenges to the reliability of an expert's conclusions, as opposed to their underlying methodology, are best left to a jury.

3. *Basis for Dr. Sung's Diagnosis*

Defendant raises an additional line of argument in its Reply,[2] that Dr. Sung's testimony is inadmissible because it is based on a flawed assumption that Plaintiff had dental extractions prior to developing ONJ. The basis for this argument is testimony from Dr. Sung suggesting that he might believe that dental extractions caused Plaintiff's ONJ: as Dr. Sung noted, Plaintiff "has a history of bisphosphonate use. There was [sic] dental procedures done on it. Again, I don't recall the dental procedure, but it predated me. And given such, she ended up with exposed bone." (Sung Dep. 233.) Defendant argues this is important because Dr. Sung has testified that ONJ will develop in a patient after undergoing a dental surgery with "almost a certainty" when on Zometa, and "[g]reater than 50 percent" when on Aredia. (Sung Dep. 75–76.) Conversely, Dr. Sung testified that spontaneous development of ONJ is "[p]robably 1 percent" when on Zometa, and "[p]robably 1 percent or less" when on Aredia. (Sung Dep. 136.) Defendant raises a valid question as to the basis of Dr. Sung's diagnosis; it is at least possible that Dr. Sung's testimony may indicate that his diagnosis was based on a mistaken belief. However, this single quote does not establish that Dr. Sung's understanding of the causation is incorrect; Dr. Sung went on to testify that, in a patient with a history of dental procedures, chemotherapy, and bisphosphonate use, he would estimate that bisphosphonate "predominantly" led to ONJ. (Sung Dep. 234). Further, Dr. Sung has not testified that Plaintiff's first lesion was ONJ, and the undisputed facts state only that Plaintiff developed a lesion preceding extraction of tooth # 31; not that this legion definitively resulted from Plaintiff's ONJ. Had Defendant raised these arguments in its original motion, Plaintiff could have responded and Defendant could have countered any of these arguments; however, the Court will not accept Defendant's argument here without it having demonstrated an absence of factual question that Dr. Sung's analysis is based entirely on a flawed assumption.

2 The Court notes that this argument should properly have been raised in Defendant's original motion, which would have given Plaintiff an opportunity to respond.

***8** Moreover, the fact that Dr. Sung believes there is about a one percent chance of ONJ developing spontaneously following years of bisphosphonate use **does not equate to a belief that there is a one percent chance that spontaneous ONJ was caused by bisphosphonate use.** In fact, Dr. Sung's estimate that about one in every one hundred people using the Treatment Drugs could develop spontaneous ONJ is extremely high, as compared with the actual incidence of ONJ in the general population. Defendant does not provide evidence suggesting that spontaneous ONJ is significantly less likely to have been caused by the Treatment Drugs; to the contrary, in its examination of Dr. Sung Defendant acknowledged that the American Association of Oral and Maxillofacial Surgeons's (AAOMS) definition of BRONJ "simply requires prior history of bisphosphonate use or current history of bisphosphonate use, exposed bone in the maxillofacial region persistent for more than eight weeks, and no history of radiation to the jaws." (Sung Dep. 235.) The Court therefore finds no basis for excluding Dr. Sung's testimony based on Dr. Sung's testimony regarding causation.

Given this, the Court DENIES Defendant's Sung Motion to exclude certain testimony.

B. *Defendant's Motion to Exclude Dr. Parisian's Testimony*

Another important Plaintiff witness in the case is Dr. Suzanne Parisian, who is designated as Plaintiff's regulatory expert. Dr. Parisian is expected to testify as to the sufficiency of Defendant's clinical research process and labeling, including whether its actions conformed with industry practice and regulatory requirements. (Parisian Mot. 1.) The Parisian Motion can be broken into eight

distinct requests. Defendant asks the Court to exclude the following anticipated testimony from Dr. Parisian: (1) that Defendant did not comply with the FDA's regulatory requirements; (2) that the Treatment Drugs should have been deemed to cause ONJ; (3) that Defendant's labeling of the Treatment Drugs after 2003 constituted an insufficient warning; (4) any testimony relating to Defendant's "state of mind"; (5) that Defendant's actions were "unreasonable" or otherwise out of compliance with industry standards; (6) that Defendant improperly conducted its clinical trials; (7) any irrelevant or unfair testimony, including that relating to any drugs other than the Treatment Drugs in this case as well as general critique of the pharmaceutical industry; and (8) that Defendant attempted to improperly influence the academic literature by "ghostwriting" articles questioning any association between the Treatment Drugs and ONJ. (*See generally* Parisian Mot.)

Defendant's arguments in support of these motions vary, but they center on three main allegations: (1) that Dr. Parisian acts as a "superlawyer" who offers legal conclusions instead of expert testimony; (2) that she testifies on subjects about which she lacks sufficient qualifications to testify; and (3) that her testimony is more prejudicial than it is probative. (Parisian Mot. 2.) In doing so, Defendant argues, she usurps the jury's function impartially deciding the facts and the Court's function stating the law, thereby confusing and misleading the jury. (Parisian Mot. 1.)

***9** Defendant also requests that the Court schedule a *Daubert* hearing. (Parisian Mot. 1.) Given the extensive briefing by the parties and the large amount of opinions and orders available from other courts discussing the admissibility of Dr. Parisian's expert testimony, the Court does not find it necessary to hold a *Daubert* hearing. *See Winter v. Novartis Pharms. Corp.*, No. 06–CV–4049, 2012 WL 827305, at *4 (W.D.Mo. March 8, 2012) ("There is an extensive amount of material available to the Court concerning Dr. Parisian and the Court does not believe a *Daubert* hearing at this late stage would be helpful or is necessary in order to rule.").

1. *Defendant's Compliance with the FDA*

Defendant's arguments seeking to exclude testimony relating to FDA compliance center on their contention that Dr. Parisian acts here as a "superlawyer," asserting legal conclusions without substantive evidentiary analysis. (Parisian Mot. 5.)

Defendant cites to the decisions of several other courts that have excluded similar testimony from Dr. Parisian in whole or in part to support its assertion that such testimony should be excluded here. *See Hogan v. Novartis Pharms. Corp.*, No. 06–CV–0260, 2011 WL 1533467, at *1–4 (E.D.N.Y. April 24, 2011); *In re Trasylol Prods. Liab. Litig.*, 709 F.Supp.2d 1323, 1351 (S.D.Fla.2010); *Miller v. Stryker Instruments*, CV 09–813–PHX–SRB, 2012 WL 1718825 (D.Ariz. Mar.29, 2012); *In re Trasylol Prods. Liab. Litig.*, 709 F.Supp.2d 1323, 1346, 1349 (S.D.Fla.2010); Parisian *Daubert* Hr'g at 126–27, 127, *Deutsch v. Novartis Pharms. Corp.*, No. 09–CV–4677 (E.D.N.Y. Apr. 11, 2011 and May 2, 2011) ("*Deutsch Daubert* Hr'g"). Not all of Defendant's case citations are instructive or on point to the case at hand. In *Hogan*, the parties agreed that the FDA was mostly irrelevant to the action and all testimony on FDA compliance was excluded. 2011 WL 1533467, at *2. In *Trasylol*, Dr. Parisian's testimony was excluded after a *Daubert* hearing, but that case did not involve the Treatment Drugs or the same report at issue here. 709 F.Supp.2d 1323. However, several courts have expressed concern that Dr. Parisian's expert reports offer impermissible legal conclusions and opinions. *See Stryker*, 2012 WL 1718825; *In re Trasylol*, 709 F.Supp. at 1346, 1349; *Deutsch Daubert* Hr'g. The Court agrees with Defendant and other courts that it is not the role of an expert witness to offer legal conclusions. *See* Fed.R.Evid. 702, 104, 403. Dr. Parisian is not permitted to offer legal conclusions on any topic, including whether Defendant was in regulatory compliance with the FDA.

The Court also notes though that many courts from the Treatment Drugs multi-district litigation have permitted Dr. Parisian to testify generally regarding FDA regulatory requirements. *See Lemons v. Novartis Pharms. Corp.*, 08–CV–00361, 2012 WL 965977, at *6 (W.D.N.C. Mar.21, 2012) (holding that, "Dr. Parisian may offer testimony only on the following issues: (1) the role, process, and function of FDA and the responsibilities of pharmaceutical drug sponsors; (2) Novartis' interactions with the FDA on the subject of labeling"); Order on Def.'s *Daubert* Mots ("*Brodie* Order"), *Brodie v. Novartis Pharms. Corp.*, No. 4:10–CV–0138 (E.D.Mo. Jan. 20, 2012) (permitting Dr. Parisian to testify on, among other topics, (1) the complex regulatory framework governing the approval, labeling, advertising, and marketing of pharmaceutical and medical products,

and (2) manufacturer responsibility and compliance with FDA regulations and guidelines); Order on Def.'s *Daubert* Mots. (*"Mahaney* Order"), *Mahaney v. Novartis Pharms. Corp.*, No. 1:06–CV–0035 (W.D.Ky. Sept. 12, 2011) (holding a *Daubert* hearing because of concerns over Dr. Parisian's Report but permitting Dr. Parisian to offer general testimony on the FDA and its drug labeling process);[3] *Deutsch,* 2011 WL 790702, at *43–44 (also holding a *Daubert* hearing because of concerns over Dr. Parisian's Report, but permitting her to testify on the general and regulatory requirements of prescription drugs by the FDA).

3 Plaintiff cites primarily to six prior court opinions within the current MDL that she believes may be instructive here. *Stevens v. Novartis Pharms. Corp.*, 358 Mont. 474, 247 P.3d 244 (Mont.2010); *Bessemer v. Novartis Pharms. Corp.*, No. MID–L–1835–08–MT (N.J. Sup.Ct. Law Div. Oct. 2010); *Fussman v. Novartis Pharm. Corp.*, No. 1:06–cv–0149, 2011 WL 5836928 (M.D.N.C. Nov.21, 2011); *Brodie* Order; *Winter v. Novartis Pharms. Corp.*, No. 3:06–CV–4049, 2012 WL 3156768 (W.D.Mo. Aug.3, 2012). The Court subsequently refers to these cases as a group, as "Plaintiff's MDL Citations."

***10** Although not bound by the decisions of these other courts, this Court finds their decisions instructive given the similarity in facts between those cases and the case at hand. The Court determines that Dr. Parisian may testify generally regarding pharmaceutical drugs within the context of the FDA. Such testimony will be helpful to members of the jury who are likely not familiar with the intricacies of FDA pharmaceutical drug approval and regulation.

Thus, the Court GRANTS IN PART and DENIES IN PART Defendant's motion to exclude Dr. Parisian's testimony on FDA compliance.

2. *Causation and Diagnosis of ONJ*

Defendant next seeks to exclude Dr. Parisian's testimony on causation or diagnosis of ONJ. As Defendant argues here, Dr. Parisian is not, and has never claimed to be, an expert on medical causation of ONJ. As such, Defendant urges this court to exclude all causation testimony from Dr. Parisian. (Parisian Mot. 8–9.)

Plaintiff agrees that Dr. Parisian is not qualified to testify as to medical causation, but responds that Dr. Parisian is not being called to testify about "medical causation," but rather will testify on regulatory "causal association." (Parisian Opp'n 15.) The distinction that Plaintiff would have this Court draw is between medical causation, which "is the result of causally randomized clinical trials," and regulatory causation, which is "not the standard of medical causation ... [but] what would trigger a manufacturer to have to change their warnings" due to causal association. Parisian *Daubert* Hr'g (*"Talley Daubert* Hr'g"), *Talley v. Novartis Pharms. Corp.*, No. 3:08–CV–0361 (W.D .N.C. June 20, 2011.

The Court is not convinced by Plaintiff's arguments distinguishing medical causation from causal association. Dr. Parisian's attempt to draw this distinction is confusing at best and would almost certainly confuse or mislead the jury. Other courts have agreed. *See Brown v. Novartis Pharms. Corp.*, No. 7:08–CV–00130, at 12, Magistrate Memorandum and Recommendation (finding "Plaintiffs' attempt to distinguish causal association from medical causation to be confusing and generally ineffective") (Index of Unpublished Cases and Court Orders for Def.'s Parisian Mot., No. 1.); *Deutsch v. Novartis Pharms. Corp.*, 768 F.Supp.2d 420, 468–69 ("Dr. Parisian is not qualified to diagnose ONJ and cannot opine on the propriety of Novartis' actions based on her own diagnosis. Accordingly, the Court grants Novartis' motion to exclude any testimony by Dr. Parisian that involves her own assessment of diagnosis or causation."). Dr. Parisian's expertise lies in issues relating to the FDA, and not in issues relating to the diagnosis or treatment of disease. **As such, she is not qualified to offer any testimony relating to the cause or diagnosis of Plaintiff's or any other patient's ONJ.** Further, allowing her to testify as to causal association would confuse the issue of causation and impermissibly allow the jury to rely on Dr. Parisian's opinion regarding the cause of Plaintiff's ONJ. The danger of unfair prejudice outweighs the probative value of this testimony.

***11 The Court GRANTS Defendant's motion to exclude Dr. Parisian's testimony on causation.**

3. *Adequacy of Labeling*

Defendant next asks the Court to exclude Dr. Parisian's testimony that the Treatment Drugs' labeling failed to timely and adequately warn doctors who prescribed these medicines. (Mot.10.) It argues that Dr. Parisian is not qualified because she is not an expert on these drugs or an oncologist who prescribes these medicines, and is

therefore unqualified to testify about how oncologists might respond to different warnings. (Parisian Mot. 10.) Defendant further argues that Dr. Parisian's testimony would be unreliable because she has not drafted any proposed alternative labeling for the Treatment Drugs. (Parisian Mot. 10–11.)

Plaintiff counters that Dr. Parisian is well qualified to testify about labeling and warnings. (Opp'n to Parisian Mot. 17.) In support of this contention, Plaintiff argues that Dr. Parisian "was involved in both drafting and reviewing product labeling while at FDA." (Parisian Opp'n 17.) Plaintiff further contends that her MDL Citations largely followed this trend, with only one case within the MDL declining to allow Dr. Parisian's testimony here. (Opp'n to Parisian Mot. 17 (referring to *Hogan v. Novartis Pharms. Corp.*, No. 06–CV–0260, 2011 WL 1533467 (E.D.N.Y. Apr. 24, 2011)).) Plaintiff also argues that although Dr. Parisian is not required to and did not provide draft labeling for the Treatment Drugs, she did state that she preferred the FDA's original drafting of the labeling. (Parisian Opp'n 17.)

The Court has already stated that Dr. Parisian's testimony as it relates to FDA requirements is admissible, and that holding applies here as well to testimony relating to FDA labeling requirements. In so holding, the Court agrees with the decisions of many other courts in this MDL that have permitted Dr. Parisian to testify on the labeling and warning of the Treatment Drugs. For example, one court observed:

> [T]he issue of adequacy of warning and labeling must be viewed, in part, in the context of the FDA's role in the approval and marketing of pharmaceuticals. Dr. Parisian's testimony on the role of the FDA and the pharmaceutical industry in general and regarding new drug approvals is relevant to establish a context in which to analyze the reasonableness of NPC's actions regarding Zometa.

Order on Mot. to Exclude Test. of Pl.'s Expert Dr. Suzanne Parisian ("*Stevens* Order"), *Stevens v. Novartis Pharms. Corp.*, No. DV–08–100, at 3 (Mont. 4th Jud. Dist.Ct. Oct. 14, 2009); *see also Fussman v. Novartis Pharms. Corp.*, No. 1:06CV149, 2011 WL 5836928, at *3 (M.D.N.C. Nov.21, 2011) (permitting Dr. Parisian to testify "as to what Novartis knew or should have known regarding the risks of ONJ and the corresponding failure of Novartis to provide an adequate warning of those risks"); *Lemons v. Novartis Pharms. Corp.*, 849 F.Supp.2d 608, 615 (W.D.N.C.2012) (permitting Dr. Parisian to testify on the issue of Novartis' interactions with the FDA on the subject of labeling). Although Defendant cites to several cases that excluded Dr. Parisian's testimony about the adequacy of warnings and labels (*see* Parisian Mot. 10 n. 12 (citing *Oakberg v. Zimmer, Inc.*, No. CV–03–47, 2004 WL 5503779, at *2 (D.Mont. Nov. 23, 2004), *Reece v. Astrazeneca Pharms., LP*, 500 F.Supp.2d 736, 745, *and Barnes Order*, at 1)), those decisions involved medical devices or drugs that are different from those at issue in this case. This limits their persuasive value, and the Court treats them accordingly. **Plaintiff may testify as to the adequacy of warnings and labels.**

***12** The Court is not convinced that Dr. Parisian has the expertise to testify how treating physicians might react to different labeling, however, particularly in light of Defendant's caselaw citations. (Parisian Mot. 10 n. 13.) Several cases have excluded speculative expert testimony relating to what decisions the experts thought prescribing doctors would have made if the drugs had different labels. *In re Diet Drugs Prods. Liab. Litig.* MDL No. 1203, 2001 WL 454586, at *18 (E.D.Pa. Feb.1, 2001); *In re Rezulin Prods. Liab. Litig.*, 309 F.Supp.2d 531, 557 (S.D.N.Y.2004)). Another case excluded Dr. Parisian's testimony "on matters of which she has no knowledge, such as actions of [the treating oncologist] and other doctors' understanding of the Zometa label". *Stevens* Order 3. The Court agrees with this line of cases that such testimony is speculative and goes beyond Dr. Parisian's knowledge. **Dr. Parisian may not offer testimony as to what decisions prescribing doctors would have made had they been given different labeling.**

Finally, the Court addresses the question whether Dr. Parisian is required to draft an alternative labeling for the Treatment Drugs. Neither party has cited binding authority delineating whether an expert witness is required to provide alternative labeling. The Court in *Brown v. Novartis Pharmaceuticals Corp.* addressed the same issue in its Memorandum and Recommendation and denied Defendant's request to exclude Dr. Parisian's testimony on labeling. (Index of Unpublished Cases and Court Orders for Defendant's Parisian Mot. Ex. 3. ("*Brown* Order"), at 12). *Brown* cites to two other cases, upon

which Defendant also relies, that require expert witnesses to draft an alternative warning label. *See Bourelle v. Crown Equip. Corp.*, 220 F.3d 532, 539 (7th Cir.2000); *Jaurequi v. Carter Mfg. Co.*, 173 F.3d 1076, 1084 (8th Cir.1999). This Court agrees with the court in *Brown*, which distinguished Dr. Parisian from the experts in those cases who talked "off the cuff" or suffered from a "level of disconnectedness" (*Brown* Order at 14.) Defendant also cites *Oswalt v. Resolute Industries, Inc.*, No. 08–CV–1600, 2010 WL 519736 (W.D.Wash. Feb.4, 2010), *rev'd on other grounds*, 642 F.3d 856 (9th Cir.2011), where the court granted summary judgment on an inadequate warning claim when plaintiff's expert failed to provide an "alternate hypothetical warning that would have been effective." *Oswalt*, 2010 WL 519736, at *3. However, the court in *Oswalt* took issue with the fact that the plaintiff's expert had not considered **any** alternative language, not with his failure to draft his own language. Here, Dr. Parisian has not only considered alternative warnings, she has even cited to an alternative (the FDA-proposed text) that she says would have been sufficient. Thus, there is no basis for excluding her testimony on this ground.

Based on the above, the Court GRANTS IN PART and DENIES IN PART Defendant's Motion to exclude Dr. Parisian's testimony on labeling and warnings of the Treatment Drugs.

4. *State of Mind*

***13** Defendant seeks to exclude Dr. Parisian's opinions about Defendant, the FDA and any person's state of mind. (Parisian Mot. 11.) Plaintiff states that Dr. Parisian will not be asked any questions regarding any party's state of mind and will not offer opinions about any party's state of mind. (Parisian Opp'n 19.) Plaintiff appears to concede this point, and so **Dr. Parisian is not permitted to testify at trial on issues related to intent or state of mind.**

The Court GRANTS Defendant's motion to exclude Dr. Parisian's state of mind testimony.

5. *Reasonableness of Defendant's Conduct and Whether it Followed Industry Standards*

Defendant next asks the Court to exclude testimony by Dr. Parisian that Defendant failed to act reasonably or follow unspecified industry standards, arguing that she is unqualified to discuss pharmaceutical companies' operating procedures and standards. (Parisian Mot. 11.) Plaintiff argues that Dr. Parisian should be permitted to testify as to the reasonableness of Defendant's actions in the context of FDA regulations, but provides no justification for this argument other than her MDL Citations. (Opp'n to Parisian Mot. 19.)

The court in *Deutsch* addressed the same issue in its opinion and excluded Dr. Parisian's opinions on the ethical standards in the pharmaceutical industry and on the obligations of Defendant in addition to those required by the FDA. It stated that:

> Although Dr. Parisian may be qualified to opine on the actions of a pharmaceutical company as it relates to its interactions with the FDA, Dr. Parisian is not qualified to opine on the ethical standards in the pharmaceutical industry, nor is she qualified to testify as to any obligations Novartis may have had to the medical community in addition to the FDA requirements.

The Court has determined above that Dr. Parisian is allowed to testify on Defendant's conduct in the context of the FDA. Plaintiff has not provided any justification for allowing Dr. Parisian to testify as to Defendant's conduct outside the context of the FDA, however. **To the extent Dr. Parisian's Report refers to industry standards that are separate or different from those of the FDA, the Court determines that Dr. Parisian is not qualified to testify as to whether Defendant complied with those standards.** *Deutsch v. Novartis Pharms. Corp.*, 768 F.Supp.2d 420, 468 (E.D.N.Y.2011).

Thus, the Court GRANTS Defendant's motion to exclude Dr. Parisian's testimony on whether Defendant followed non-FDA industry standards.

6. *Clinical Trials*

Defendant seeks to exclude Dr. Parisian's opinion testimony that Defendant failed to adequately monitor clinical trial safety. (Parisian Mot. 12.) Plaintiff also does not contest this section of the Parisian Motion. Instead, she claims that Dr. Parisian has never before been asked any questions about Defendant's failure to adequately monitor its clinical trials during cases within this MDL, restricting her testimony to opinions on their conduct and reporting of results. (Parisian Opp'n 19.) **As such, Dr.**

Parisian is not permitted to testify at trial on the issue whether Defendant adequately monitored its clinical trials.

***14 The Court GRANTS Defendant's motion to exclude Dr. Parisian's testimony regarding clinical trials.**

7. *Other Drugs and Post-injury Actions*

Defendant further argues that Dr. Parisian should not be permitted to testify on events occurring after Plaintiff's exposure to the Treatment Drugs, and on events regarding other drugs. (Parisian Mot. 12.) Specifically, it seeks to exclude testimony on (1) Dr. Parisian's criticism of the FDA and the pharmaceutical industry that does not relate to the Treatment Drugs; (2) drugs other than the Treatment Drugs that have caused ONJ; (3) injuries other than ONJ that have resulted from the Treatment Drugs; and (4) events that occurred after Plaintiff stopped taking Zometa in March 2005. (Parisian Mot. 12.) Defendant argues such testimony would be irrelevant, unfairly prejudicial, and confusing. (Parisian Mot. 12.)

Plaintiff has not addressed Defendant's arguments in her Opposition. The Court agrees with Defendant that the probative value of testimony on drugs other than the Treatment Drugs and injuries other than ONJ is outweighed by the danger of unfair prejudice, because it could contribute to a negative overall view of Defendant's drug manufacturing activities. To the extent events that occurred after Plaintiff stopped taking Zometa in March 2005 are unrelated to her use of Zometa, this testimony is also excluded because the danger of unfair prejudice outweighs its probative value.

The Court GRANTS Defendant's motion to exclude Dr. Parisian's testimony regarding drugs other than the Treatment Drugs, and on events after Plaintiff stopped taking Zometa.

8. *Ghostwriting*

Finally, Defendant asks the Court to exclude Dr. Parisian's testimony regarding ghostwriting and company funding of publications. (Parisian Mot. 12.) Again, Plaintiff does not object to this section of the Parisian Motion. (Parisian Opp'n 20.) As such, Dr. Parisian is not permitted to testify at trial on the topic of ghostwriting.

The Court GRANTS Defendant's motion to exclude Dr. Parisian's testimony regarding ghostwriting.

C. *Defendant's Motions to Exclude Dr. Marx's Testimony*

Defendant next asks the Court to exclude certain testimony from Dr. Robert Marx, who Plaintiff has designated as her expert on general causation issues, as well as on Defendant's conduct in conducting its clinical trials and determining the safety of the Treatment Drugs. Defendant seeks to exclude the following testimony by Dr. Marx: (1) whether dental evaluation and treatment measures are effective in preventing BRONJ; (2) Defendant's alleged "bad faith" conduct; (3) criticism of Defendant's clinical trials; (4) whether certain patients in clinical trials had BRONJ; (5) general causation testimony based on adverse events reports; and (6) the biological mechanism by which BP drugs allegedly cause ONJ. (*See generally* Marx Mot.) Defendant provides different reasons for each of these requests. It does not challenge the admissibility of Dr. Marx's testimony on general causation.

1. *Preventing BRONJ Through Dental Evaluation and Treatment*

***15** Defendant first asks the Court to preclude Dr. Marx's opinion that obtaining a dental examination before starting BP therapy and avoiding oral surgery (including tooth extractions) while on BP drugs can prevent BRONJ. (Marx Mot. 3.) Defendant argues that Dr. Marx has no basis for his testimony, and that therefore any opinions he has on the preventative value of dental treatment measures are "speculative belief," not admissible as expert testimony. (Marx Mot. 4.)

Defendant does not cite any case from the multi-district litigation involving the Treatment Drugs that excluded Dr. Marx's testimony on this topic. To the contrary, this Court found multiple decisions from other courts within the MDL addressing the substantially similar issue of the admissibility of Dr. Marx's testimony on preventative measures of BRONJ, and declining to exclude this evidence. In *In re Aredia & Zometa Products. Liability Litigation,* the Middle District of Tennessee found that Dr. Marx's testimony was admissible under *Daubert* relating to (1) the causal connection between the Treatment Drugs and ONJ, and (2) treatment and preventative measures for ONJ. No. 3:06–MD–1760, Order of Def.'s Mot to Exclude Litigation–Wide Test. of Pl.'s Expert Dr. Robert Marx, D.D.S. (M.D.Tenn. Aug. 13, 2009) (mentioned in Girardi Decl. Ex. 1). Similarly, in

Bessemer, like in this case, Novartis sought to prevent Dr. Marx's testimony that certain dental treatment measures are effective in preventing BRONJ. The court found that:

> Dr. Marx's opinion is based on scientific literature and his own clinical experience treating patients with BRONJ. To the extent that there is conflicting evidence regarding the effectiveness of dental treatment measures in preventing BRONJ, Defendant will be able to crossexamine this witness. As such, the court will not exclude Dr. Marx's testimony.

Bessemer v. Novartis Pharms. Corp., No. MID–L–1835–08 (N.J. Sup.Ct. Law Div. Oct. 2010) (Girardi Decl. Ex. 3, at 3). In *Hogan v. Novartis Pharmaceuticals Corp.*, the court noted that the "MDL Court has already found Dr. Marx qualified to opine on general and specific causation as well as on treatment and preventive measures for ONJ." (No. 06–CV–0260, 2011 WL 1533467, at *4 (E.D.N.Y. Apr.24, 2011); *see also Mahaney* Order 28–29) (permitting testimony on preventive dental treatment for BRONJ and stating that Dr. Marx's testimony "may be thoroughly vetted on cross examination" by Defendant); *Deutsch v. Novartis Pharms. Corp.*, 768 F.Supp.2d 420, 438 ("The theory that preventative measures, including pretreatment dental screening, may decrease the risk of [BRONJ] is admissible and it is well within ... [Dr. Marx's] field of expertise").

Although not binding on this Court, the decisions of other courts who have addressed the admissibility of substantially the same evidence at issue in this case are persuasive and wellreasoned. Defendant is free to provide contrary evidence and attack Dr. Marx's testimony on cross examination, but has not demonstrated any basis for exclusion of Dr. Marx's testimony here.

***16 Based on the above, the Court DENIES Defendant's motion to exclude Dr. Marx's testimony on the prevention of BRONJ through dental evaluation and treatment.**

2. *Defendant's Alleged "Bad Faith" Conduct*

Defendant next asks the Court to exclude Dr. Marx's testimony on any alleged "bad faith" conduct of Defendant or opinions on Defendant's intent or motives. (Marx Mot. 4–6.) In support of this, Defendant points to Dr. Marx's testimony about one article where he notes that his testimony alleging bad faith by Defendants is his "own personal opinion." (Marx Mot. 5.) Plaintiff responds by citing to substantial caselaw (*see generally* Marx Opp'n), although Plaintiff also notes that Defendant's challenge to the "bad faith" comments is not frivolous; she argues that this testimony falls "within the purview of the jury" (Marx Opp'n 9).

Other courts in the MDL have routinely excluded such testimony on "bad faith" and state of mind, because such statements fall outside of Dr. Marx's expertise and qualify instead as personal opinion testimony. *See Hogan,* 2011 WL 1533467, at *4; *Bessemer* (Girardi Decl. Ex. 3, at 3–4); *Brodie* Order 4; *Mahaney* Order 26–33; *Winter,* 2012 WL 827305, at *5–*9; and *Deutsch,* 768 F.Supp.2d at 448. This Court agrees with this general consensus, and will not allow Dr. Marx to testify on his personal opinions.

Thus, the Court GRANTS Defendant's motion to exclude Dr. Marx's testimony on Defendant's alleged "bad faith" conduct, intent, or motives.

3. *Criticism of Defendant's Clinical Trials*

Defendant also asks the Court to exclude Dr. Marx's criticism of its clinical trials of the Treatment Drugs. (Marx Mot. 6–7.) Other courts in the Treatment Drugs cases have routinely excluded this testimony and this Court does so for the same reasons. *See Hogan,* 2011 WL 1533467, at *6 (Dr. Marx could not give testimony criticizing the design of the clinical trials); *Brodie* Order 4) (Dr. Marx was not permitted to give conclusory criticism of the clinical trials); *Bessemer* (Girard Decl. Ex. 3, at 3–4) (excluding testimony on Dr. Marx's criticism of the clinical trials, but permitting him to give factual statements about them); *Mahaney* Order 32 (Dr. Marx was not permitted to give criticism of the clinical trials); *Winter,* 2012 WL 827305, at *8 (Dr. Marx was not permitted to testify as to his opinion on the design of the clinical trials); and *Deutsch,* 768 F.Supp.2d at 450 (excluding Dr. Marx's opinions on the design and conduct of the clinical trials).

Thus, the Court GRANTS Defendant's motion to exclude Dr. Marx's testimony criticizing Defendant's clinical trials of the Treatment Drugs.

4. *Diagnosis of BRONJ in Clinical Trials Patients*

Defendant next asks the Court to exclude Dr. Marx's testimony about whether certain patients in the Treatment

Drugs clinical trials had BRONJ. (Marx Mot. 7–9.) It argues this testimony is speculative and not based on a reliable methodology because Dr. Marx abandoned the methodology he normally uses when he concluded that these patients had BRONJ. (Marx Mot. 7–9.) Plaintiff again responds with a litany of caselaw, although it argues specifically that Dr. Marx's testimony will be limited to diagnosis rates and will avoid testimony concerning the sufficiency of Defendant's process. (Marx Opp'n 9.)

***17** Defendant made substantially the same argument in *Hogan.* 2011 WL 1533467, at *5. The court there rejected Defendant's argument that Dr. Marx's conclusions were speculative and stated that "Dr. Marx's opinion on whether participants in defendant's clinical trial had BRONJ ... is both relevant and reliable." *Id.; see also Deutsch,* 768 F.Supp.2d at 450 (denying Defendant's motion to exclude Dr. Marx's testimony on whether the individuals in the clinical trials had BRONJ and stating that "[w]hile the Court finds that Dr. Marx may be overstating the results by concluding that these patients had 'likely ONJ,' Novartis is certainly free to cross-examine him on the strength of that statement and the accuracy of his results").

Thus, the Court DENIES Defendant's motion to exclude Dr. Marx's testimony diagnosing BRONJ in certain patients from the clinical trials of the Treatment Drugs.

5. *General Causation Testimony Based on Adverse Events Reports*

Defendant asks the Court to exclude Dr. Marx's general causation testimony that is based on Adverse Event Reports ("AER") submitted to the FDA or Defendant, because Dr. Marx did not review these reports, and because AERs do not constitute scientifically reliable causation proof. (Marx Mot. 9.) Plaintiff does not reply specifically to these arguments.

Defendant's arguments here are unavailing. Although Dr. Marx may not have reviewed any of the AERs, his testimony makes clear that he discussed these AERs with the FDA and relied upon their results. (Def. Ex. 15, Dep. of Robert Marx ("Marx Dep."), at 859–860.) Dr. Marx's testimony notes further that it is standard practice, because it is often difficult to obtain the original AERs. (Marx Dep. 859–60.) Turning to the sufficiency of AERs as scientific proof, Defendant cites to *McClain v. Metabolife Intern. Inc.,* 401 F.3d 1233 (11th Cir.2005), to support its contention that such reports are inadmissible. But even if its decision were binding, the court in *McClain* considered the expert's reliance on AERs as but one factor in a many-factor test to determine whether the expert's testimony was admissible under *Daubert. McClain,* 401 F.3d at 1250. This is a far cry from ruling that testimony based on AERs is inadmissible per se.

Other courts in the Drug Treatment cases have also permitted this testimony and, as above, Defendant has not cited any cases that have excluded it. *See Mahaney* 835 F.Supp.2d 299, 311–12; *Deutsch,* 768 F.Supp.2d at 450–51. Additionally, the court in *Bessemer* characterized Defendant's substantially similar challenge in that case as "overly broad and vague" and stated that it would await the trial testimony to determine whether Dr. Marx relied on adverse event reports in forming his opinion. (Girardi Decl. Ex. 3, at 4).

For all of these reasons, the Court DENIES Defendant's motion to exclude Dr. Marx's general causation testimony based on adverse events reports.

6. *Biological Mechanism by Which BP Drugs Allegedly Cause ONJ*

***18** Finally, Defendant seeks to exclude Dr. Marx from testifying on the biological mechanism by which BP drugs allegedly cause ONJ. (Marx Mot. 10.) Once again, the Court finds the decisions of other courts involved in the Drug Treatment cases persuasive and agrees with their findings admitting this testimony. *See Bessemer* (Girardi Decl. Ex. 3, at 4) ("Dr. Marx has offered sufficient expertise and reliability to offer his opinion" on this topic); *Deutsch,* 768 F.Supp.2d at 438 ("The Court has no doubt that [Dr. Marx's] academic involvement and extensive background in identifying, treating, and studying patients with ONJ qualifies him to render opinions on this subject."). Defendant has provided no meritorious argument to exclude this testimony that would run counter to the general caselaw on this point. [4]

4 The Court is similarly unconvinced by Defendant's argument that studies on mice cells are irrelevant to knowledge of how human cells work, which line of argument Defendant also attempted in its Sung Motion. If mouse cell activity were irrelevant to greater understanding of human cell activity, no one would study mouse cells. Defendants may argue in their cross examination that the study is an indirect indicator of human cell activity, but these arguments

> go to the strength of Dr. Marx's testimony, not to its admissibility.

Based on the above, the Court DENIES Defendant's motion to exclude Dr. Marx's testimony on the biological mechanism by which BP drugs allegedly cause ONJ.

III. *RULING*

For the foregoing reasons, the Court **DENIES DEFENDANT'S SUNG MOTION; GRANTS IN PART AND DENIES IN PART DEFENDANT'S PARISIAN MOTION;** and **GRANTS IN PART AND DENIES IN PART DEFENDANT'S MARX MOTION.** Dr. Sung may testify as designated by Plaintiff in full. Dr. Parisian may testify as to FDA regulatory compliance and the adequacy of Defendant's labels and warnings. Dr. Parisian may not testify as to (1) causation, regulatory or otherwise; (2) how prescribing doctors would have responded to different labeling; (3) Defendant's or any other party's "state of mind"; (4) the reasonableness of Defendant's actions, or whether they complied with industry standards; (5) the propriety of Defendant's clinical trials; (6) any drugs other than the Treatment Drugs or any actions occurring after Plaintiff stopped treatment; or (7) Defendant's alleged "ghostwriting" of articles. Dr. Marx may testify as to (1) the effectiveness of dental treatment; (2) the diagnoses from Defendant's clinical trials; (3) the findings of Adverse Event Reports; and (4) the biological mechanism by which BP drugs cause ONJ. Dr. Marx may not testify as to Defendant's "bad faith" conduct, or the propriety of Defendant's clinical trials.

IT IS SO ORDERED.

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Exhibit O

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United States District Court, S.D. Florida,
Miami Division.

In re DENTURE CREAM PRODUCTS LIABILITY LITIGATION.
This Document Relates to Case No. 9:09–CV–80625–CMA (Chapman, et al. v. Procter & Gamble Distributing LLC).

No. 09–2051–MD.
|
July 22, 2011.

ORDER

CECILIA M. ALTONAGA, District Judge.

***1 THIS CAUSE** came before the Court on Defendant, the Procter & Gamble Distributing LLC's ("Procter & Gamble['s]") motions to exclude all or part of the testimony of seven of Plaintiff, Marianne Chapmans' expert witnesses. (*See* [ECF Nos. 1040–1044]). The proposed testimony covers a variety of topics. The majority of the discussion in this Order focuses on the Motion to Exclude the Opinions of Plaintiffs' Experts Drs. Brewer, Greenberg, and Landolph ("Brewer Motion") [ECF No. 1040], and the Motion to Exclude the Opinions of Plaintiffs' Expert Dr. Ebbing Lautenbach ("Lautenbach Motion") [ECF No. 1041], each filed on April 1, 2011.[1] The proposed testimony of Drs. Brewer, Landolph, and Lautenbach concerns whether Fixodent is, in general,[2] capable of causing a copper-deficiency myelopathy;[3] while Dr. Greenberg's proposed testimony addresses the specific question of whether Plaintiff, Marianne Chapman's myelopathy was caused by her use of Fixodent.[4] The Court has carefully considered the Motions; the thousands of pages of filings by the parties, including the experts' reports and depositions, and scientific literature; as well as oral argument by the parties, a broad variety of secondary literature on the use of scientific evidence in the courtroom, and the law.

1 Dr. Brewer is Plaintiffs' expert on zinc metabolism, Dr. Landolph is a toxicologist, and Dr. Lautenbach is an epidemiologist.

In other motions, Defendant also seeks to exclude the testimony of Dr. Frederick Raffa ("Raffa Motion") [ECF No. 1042], portions of the testimony of Dr. J. Anthony Von Fraunhofer ("Fraunhofer Motion") [ECF No. 1043], and the testimony of Dr. Michael S. Wogalter ("Wogalter Motion") [ECF No. 1044], all filed on April 1, 2011. Defendant does not challenge the Report (*see* [ECF No.1072–14]) of Dr. Prohaska, Plaintiffs' biochemist, linking copper deficiency and blood disorders.

2 " 'General causation is concerned with whether an agent increases the incidence of disease in a group and not whether the agent caused any given individual's disease.' " *McClain v. Metabolife, Int'l., Inc.*, 401 F.3d 1233, 1239 (11th Cir.2005) (quoting Michael D. Green *et al., Reference Guide on Epidemiology,* in REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 392 (Federal Judicial Center, 2d ed.2000) [hereinafter Green, REFERENCE MANUAL])).

3 A number of different terms have been used —more or less as synonyms, regardless whether that is medically accurate—in the course of the litigation to refer to a constellation of neurological injuries allegedly caused by long-term use of Fixodent. Those terms include myelopathy, myeloneuropathy, myelopolyneuropathy, copper-deficiency myelopathy, peripheral neuropathy, CNS demyelination, axonal polyneuropathy, and others.

4 Dr. Von Fraunhofer, a dental technologist, also makes the link between Fixodent and myelopathy (*see* Von Fraunhofer Rep. [ECF No. 1046–5]), but he is not a primary witness on general causation. Dr. Von Fraunhofer bases his causation conclusion on two case reports. (*See* Von Fraunhofer Rep. 15 (citing Nations *et al., Denture cream: An unusual source of excess zinc, leading to hypocupremia and neurologic disease,* NEUROLOGY, 71:639–643 (June 2008) (the "Nations Article"), and Hedera et al., *Myelopolyneuropathy and pancytopenia due to copper deficiency and high zinc levels of unknown origin II,* NEUROTOXICOLOGY (2009) (the "Hedera Article"). As will become apparent, the basis of his general causation inference is subject to the same reliability concerns as arise with Drs. Brewer, Landolph, and Lautenbach.

I. BACKGROUND

Thirty-three year old Marianne Chapman suffers from a constellation of neurological symptoms that evolved during a 2.5 year period from April 2006 to January 2009. (*See* Greenberg Rep. 4 [ECF No. 1047–1]). These symptoms began in 2006 when she developed a numbness in her fingertips, followed a month later by numbness in both feet.[5] (*See id.*). Eventually, "all feeling in the hands and feet were lost, pins and needles parasthesis were [sic] present, and pain with light touch in the feet was prominent." (*Id.*). From June 2006 to January 2008, Ms. Chapman developed a progressive gait ataxia, which first caused her to trip frequently while walking in the dark, and then kept her confined to bed for fear of falling while walking. (*See id.*). A burning pain in her hands and feet intensified during this period and required management with opiods. (*See id.*). In July 2006, she was discovered to have blood dyscrasias, including anemia and neutropenia (low red and white blood cell counts). (*See id.*). Around January 2008, Ms. Chapman developed "subacute bilateral asymmetric wrist and finger drop," which intensified in both hands over a several-month period and limited her ability to extend her fingers and thumbs. (*Id.*).

5 Dr. Greenberg notes, but considers unrelated, a March 2004 visit to the doctor, at which Ms. Chapman complained of numbness along the right lateral leg. She was discovered to have a vitamin B12 deficiency, was treated for that deficiency, and the leg numbness resolved. (*See* Greenberg Rep. 4).

Plaintiffs contend Ms. Chapman's symptoms are the result of zinc-induced copper-deficiency myelopathy brought on by her use of two to four 68–gram tubes[6] of Fixodent denture adhesive every week for eight years to hold her dentures in place. (*See* Brewer Opp'n [ECF No. 1071]; *see also* Greenberg Rep. 8). In contrast, Procter & Gamble maintains the methodologies used by Plaintiffs' experts to conclude that Fixodent can cause myelopathy and that Fixodent caused Ms. Chapman's neurological problems are unreliable, and thus the experts' testimony should not be admitted.

6 The 68–gram tube is about the size of a medium-sized tube of toothpaste.

***2** After Defendant filed its *Daubert* motions, additional deposition testimony was taken from the experts. The Defendant was then permitted to supplement its *Daubert* motions based on those depositions. (*See* [ECF No. 1037]). Plaintiffs were permitted to respond to those supplemental briefs.

II. LEGAL STANDARD

Federal Rule of Evidence 702, which governs expert testimony, states as follows:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

Rule 702 requires district courts to ensure "that an expert's testimony both rests on a reliable foundation and is relevant to the task at hand." *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 597 (1993). This "gatekeeping" function must be performed with regard to the admissibility of both expert scientific evidence and expert technical evidence. *See United States v. Frazier*, 387 F.3d 1244, 1260 (11th Cir.2004) (citing *Daubert*, 509 U.S. at 589 n. 7 & 597; *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 147 (1999)). "This function inherently requires the trial court to conduct an exacting analysis of the *foundations* of expert opinions to ensure they meet the standards for admissibility under Rule 702." *Id.* (alterations and internal quotation marks omitted).

In determining the admissibility of expert testimony, the Eleventh Circuit requires district courts to conduct a three-part inquiry about whether:

> (1) the expert is qualified to testify competently regarding the matters he intends to address; (2) the methodology by which the expert reaches his conclusions is sufficiently reliable as determined by the sort of inquiry mandated in *Daubert;* and (3) the testimony assists the trier of fact, through the applications of scientific, technical, or specialized expertise, to understand the evidence or to determine a fact in issue.

Hendrix ex rel. G.P. v. Evenflo Co., 609 F.3d 1183, 1194 (11th Cir.2010) (citing *Frazier,* 387 F.3d at 1260). The burden is on the proponent of the expert testimony to show, by a preponderance of the evidence, that the testimony satisfies each prong. *See id.* (citing *Boca Raton Cmty. Hosp., Inc. v. Tenet Health Care,* 582 F .3d 1227, 1232 (11th Cir.2009)). In this case, as in *Hendrix,* only the second prong—reliability—is in dispute. *See id.*

In *Daubert,* the Supreme Court suggested a non-exhaustive list of several factors to consider in determining if a specific methodology is reliable under Rule 702: whether the methodology can and has been tested; whether the methodology has been subjected to peer review and publication; the known or potential rate of error and the existence and maintenance of standards controlling operation of the methodology; and whether the methodology has gained general acceptance in the scientific community. *See Daubert,* 509 U.S. at 593–94 (declining to set forth a "definitive checklist or test"); *accord Kumho,* 526 U.S. at 141. In *Kumho,* the Supreme Court emphasized, "the trial judge must have considerable leeway in deciding in a particular case how to go about determining whether particular expert testimony is reliable." *Kumho,* 526 U .S. at 152. Nevertheless, while the inquiry is "a flexible one," the focus "must be solely on principles and methodology, not on the conclusions that they generate." *Daubert,* 509 U.S. at 594–95. "But conclusions and methodology are not entirely distinct from one another ... [and] nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert." *Gen. Elec. Co. v. Joiner,* 522 U.S. 136, 146 (1997). "Rather, the trial court is free to 'conclude that there is simply too great an analytical gap between the data and the opinion proffered.' " *Hendrix,* 609 F.3d at 1194 (citing *Joiner,* 522 U.S. at 146).

III. ANALYSIS

***3** Doctors Brewer, Landolph, and Lautenbach, each to a greater or lesser extent and despite coming from different disciplines, rely on the same information, predominantly case studies, to conclude the use of very large amounts of Fixodent over a very long period of time can cause a class of neurological diseases called myelopathy.[7] Because Drs. Brewer, Landolph, and Lautenbach use the same information to infer general causation, the Court addresses the admissibility of their proposed testimony together in section III.A of this Opinion. In section III.B, the Court addresses the testimony of Dr. Greenberg, Plaintiffs' expert on specific causation, who concludes it was Marianne Chapman's use of Fixodent that caused her to develop zinc-induced copper-deficiency myelopathy. In section III.C, the Court addresses Defendant's motions to exclude the testimony of Drs. Wogalter, Von Fraunhofer, and Raffa.

7 A myelopathy is any "disturbance or disease of the spinal cord ." THE AMERICAN HERITAGE MEDICAL DICTIONARY (Houghton Mifflin 2007); (*see also* Greenberg Dep. 23:8–9 [ECF No. 1137–3] ("Myelopathy is a category of conditions that affect the spinal cord.")).

A. General Causation: Whether Plaintiffs' Experts Use a Reliable Scientific Methodology to Conclude Fixodent Can Cause a Myelopathy.

In *McClain,* the Eleventh Circuit noted "toxic tort cases usually come in two broad categories: first, those cases in which the medical community generally recognizes the toxicity of the drug or chemical at issue, and second, those cases in which the medical community does not generally recognize the agent as both toxic and causing the injury plaintiff alleges."[8] *McClain,* 401 F.3d at 1239. Not surprisingly, the parties dispute the proper categorization of the agent[9] in this case; however, for reasons that are explored in great detail below, this case falls into the second category because there is no reliable basis

to conclude either Fixodent or zinc can cause copper-deficiency myelopathy.

8 Some examples of known toxic agents that the Eleventh Circuit highlights are "asbestos, which causes asbestosis and mesothelioma; silica, which causes silicosis; and cigarette smoke, which causes cancer." *McClain,* 401 F.3d at 1239. The alleged association between the zinc in Fixodent and copper-deficiency myelopathy does not have the same widespread acceptance by the medical community as the Eleventh Circuit's examples.

9 The categorization is complicated because the parties disagree about what the agent or chemical at issue is. It is Plaintiffs' view that they need only show that zinc can cause copper-deficiency myelopathy and that Fixodent contains absorbable zinc, while Defendant argues Plaintiffs must show that Fixodent can cause a copper-deficiency myelopathy.

Plaintiffs submit the testimony of three experts—Drs. Brewer, Landolph, and Lautenbach—in an attempt to establish that Fixodent is capable of causing a myelopathy. Dr. Brewer would testify "that zinc containing Fixodent denture adhesives are a health hazard and capable of causing severe hematological and neurological injury." (Brewer Rep. [ECF No. 1046–1]). Dr. Landolph would testify "that long-term use of Fixodent (containing 1.69% zinc) will result in ... neurotoxic, neurologic, and hematologic consequences." (Landolph Rep. [ECF No. 1046–7]). Dr. Lautenbach, whose opinion is expressed in a rebuttal report, would testify, somewhat tepidly, that there is "an association between Fixodent and myeloneuropathy" and he would "consider the myeloneuropathy as a 'probable' reaction related to denture adhesive use." (Lautenbach Rep. ¶¶ 40, 45 [ECF No. 1046–9]). [10]

10 Dr. Greenberg would testify, "[b]etween 2007–2009, several publications established that zinc poisoning from certain denture adhesive creams are the most common cause of copper-deficiency myelopathy." (Greenberg Rep. 1 (referencing five case-report articles)). He relies heavily on the Hedera Article. (*See id.* ("[O]ne research group re-interviewed their previous 11 patients with elevated zinc levels and copper deficiency and discovered that all 11 were denture cream users.")).

1. Reliable Methodologies

A survey of Eleventh Circuit *Daubert* jurisprudence in toxic-tort cases identifies several types of evidence and methodologies that have been described as reliable bases for an inference of general causation. Those types of evidence and methodologies are drawn from toxicology and epidemiology and include the dose-response relationship, [11] epidemiological studies, [12] the amount of background risk of the disease, [13] an understanding of the physiological mechanisms involved, and clinical studies or tests. *See* Green, REFERENCE MANUAL 374–379. A plaintiff need not provide evidence of each above-described type, but an inference of general causation that is made in the absence of any of these preferred types of evidence has been and will be deemed unreliable in this Circuit.

11 The dose-response relationship is "[a] relationship in which a change in amount, intensity, or duration of exposure to an agent is associated with a change—either an increase or decrease—in risk of disease." *McClain,* 401 F.3d at 1241–42 (citing Green, REFERENCE MANUAL 390). "The expert who avoids or neglects [the dose-response] principle of toxic torts without justification casts suspicion on the reliability of his methodology." *Id.* at 1242.

12 Epidemiology, a field that concerns itself with finding the causal nexus between external factors and disease, is generally considered to be the best evidence of causation in toxic tort actions.' " *Kilpatrick v. Breg, Inc.*, 613 F.3d 1329, 1337 n. 8 (11th Cir.2010) (quoting *Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194, 1198 (11th Cir.2002)).

13 Background risk is "[t]he risk a plaintiff and other members of the general public have of suffering the disease or injury that the plaintiff alleges *without* exposure to the drug or chemical in question." *McClain,* 401 F.3d at 1242 (alteration and emphasis in original). "A reliable methodology should take into account the background risk." *Kilpatrick,* 613 F.3d at 1342 (quoting *McClain,* 401 F.3d at 1243–44).

a. Dose–Response

***4** "All substances are poisonous—there is none which is not; the dose differentiates a poison from a remedy." David Eaton, *Scientific Judgment and Toxic Torts: A Primer in Toxicology for Judges and Lawyers,* 12 J.L. & POL'Y 1, 11 (2003) [hereinafter Eaton] (quoting CASARETT AND DOULL'S TOXICOLOGY: THE BASIC SCIENCE OF POISONS Chs. 1, 4 (McGraw Hill

6th ed.2001) (quoting the 16th Swiss–German Physician/ Philosopher Paracelsus)). Because all substances have the potential to be toxic, " 'the relationship between dose and effect (dose-response relationship) is the hallmark of basic toxicology,' " *McClain,* 401 F.3d at 1242 (quoting Eaton 15), and " 'is the single most important factor to consider in evaluating whether an alleged exposure caused a specific adverse effect' " *id.* (quoting Eaton 11). " '[F]or most types of dose-response relationships following chronic (repeated) exposure, thresholds exist, such that there is some dose below which even repeated, long-term exposure would not cause an effect in any individual.' " *Id.* (quoting Eaton 16). Often " 'low dose exposures—even for many years—will have no consequence at all, since the body is often able to completely detoxify low doses before they do any damage." *Id.* (quoting Green 13). This last statement is almost certainly true of Fixodent, which, as even Plaintiffs seem to concede, is safe when used in moderate amounts. (*See* Hr'g Tr. 134:9–135:24).

Nevertheless, Fixodent and the zinc it contains, like water and oxygen, [14] are potentially toxic. Common sense suggests that one would expect consuming three-fifths of a pound [15] of denture cream per week for eight years would have some type of negative consequence. "Thus, the question for causation purposes is: At what levels of exposure do what kinds of harm occur?" *Cavallo v. Star Enter.,* 892 F.Supp. 756, 769 n. 27 (E.D.Va.1995), *rev'd on other grounds, Cavallo v. Star Enter.,* 100 F.3d 1150, 1157–59 (4th Cir.1996). In this case, Plaintiffs' experts contend the use of Fixodent in a particular way causes a particular disease—specifically, Plaintiffs' experts conclude extremely large amounts of Fixodent applied to dentures several times a day for a period of many years can cause copper-deficiency myelopathy.

14 *See, e.g.,* DJ Farrell *et al., Fatal water intoxication,* 56(10) J. CLIN. PATHOL.. 803 (2003); C. Acott, *Oxygen Toxicity: A brief history of oxygen in diving,* 29(3) S. PAC. UNDERWATER MED. SOC. 150 (1999).

15 Four 68–gram tubes of Fixodent are roughly equal to .6 pounds of Fixodent.

Yet, neither Plaintiffs' experts nor the articles on which they rely determine how much Fixodent must be used for how long to increase the risk of a copper-deficiency, or for how long a copper-deficiency must persist before an individual is at an increased risk of developing a myelopathy. [16] Plaintiffs argue Dr. Brewer's Wilson's disease [17] research establishes some people are placed into a negative copper balance with a single 25 mg dose of zinc. (*See* Brewer Opp'n 10). While this may be true, there is a large analytical gap between the proposition that a 25 mg dose of zinc may, at a given time, place a particular person into a temporary negative copper balance, to the proposition that some people who ingest 25 mg of zinc per day for many years will develop a severe copper deficiency with neurological symptoms. Dr. Brewer's Wilson's disease experiments do establish what dose of Galzin, or zinc acetate, is necessary to induce a negative copper balance (*see* Brewer Rep. 4); however, the Procter & Gamble pharmacokinetic studies indicate that the zinc in Fixodent is less bio-available than that in zinc acetate. (*See* PK Study 35 [ECF No. 1072–1]). [18]

16 Dr. Brewer:

Q. Have you ever determined the dose of Fixodent necessary to consistently place individuals into a negative copper balance?

A. Experimentally, no.

(Brewer Dep. 108:8–11 [ECF Nos. 1087–1, 1137–4]; *see also id.* 109:10–12, 177:14–18).

* * *

Q. But you're unable to tell us how long it has to be that low to cause myelopolyneuropathies or myelopathies?

A. Yeah. I can tell you that it will not happen in the first couple of weeks.

Q. Okay.

A. But I don't know how long it takes to happen.

(*Id.* 60:1–8).

Dr. Lautenbach:

Q. Now, do you know how much below normal copper has to be, serum copper has to be and for how long before you have myelopathies?

A. I don't know.

(Lautenbach Dep. 62:5–9 [ECF No. 1137–1]). Dr. Landolph:

Q. So no studies have been done to determine how low the copper must be in the serum and for how long to cause myelopathy?

A. I had not seen such a precise curve ....

(Landolph Dep. 43:3–8 [ECF No. 1087–2]).

Hedera Article: "We could only estimate daily zinc exposure ... [because] the bioavailability of zinc from denture cream is unknown." (Hedera Article 2; *see also* Hedera Dep. 263:11–14 [ECF No. 1137–6] ("I don't have a good date to how long does it

take to—to—to develop problems; so we didn't go into such details.")).

17 In Wilson's disease there is too much copper in the body's tissues.

18 Dr. Brewer also acknowledged this:

> Q. Exposure to a polymer matrix does not equate to exposure to the individual components of the polymer matrix, does it?
> A. Are you referring to oral ingestion of such?
> Q. Yep.
> A. In that case, no, it doesn't. They don't correspond directly.

(Brewer Dep. 78:13–20).

***5** Moreover, one cannot simply figure out the dose of zinc from Fixodent by doing some simple arithmetic [19] based on the pharmacokinetic studies because, apparently to the surprise of the investigators in that study, a 6 g dose of Fixodent only delivered slightly more bio-available zinc than the 3 g dose. (*See* PK Study 35) ("[S]ystemic exposures from Fixodent 6 g were not markedly greater than Fixodent 3 g even though the 6 g product had twice the amount of elemental zinc (100 mg versus 50 mg) relative to the 3 g product."). This suggests taking more and more Fixodent may not expose someone to more and more zinc; that is, there may be some limiting factor due to the composition of Fixodent, human biology, or something else. [20]

19 Plaintiffs disagree:

> We know, even based on their numbers in the pharmacokinetic study that there is a relative bioavailability of the zinc in Fixodent compared to the 25 milligram zinc acetate supplement. So we can *easily make a ready comparison,* as Dr. Landolph did, the toxicologist, and show she was consuming huge amounts of zinc.

(Hr'g Tr. 93:14–19) (emphasis added).

20 Another hole in the dose-response picture is that, with the exception of the primogenital case report of a man who was eating pellets of Poligrip, most of the case-study subjects and Ms. Chapman applied denture cream to their dentures in very large amounts but for its intended purpose—to hold their dentures in place. Some of the excess would ooze out immediately and some of the remainder would wash out or be swallowed with food between applications. In order to obtain a reliable understanding of Fixodent's actual effect on copper balance, the product's actual usage patterns should be modeled in tests to determine if it is capable of delivering zinc in a way that will cause a negative copper balance and, within ethical limits, a copper deficiency.

For these reasons, one cannot reliably infer from Dr. Brewer's Galzin studies how much Fixodent is necessary to consistently induce a negative copper balance. Accordingly, there is no dose-response evidence which Plaintiffs' experts may use to reliably infer what type of exposure level to Fixodent is necessary to induce a negative copper balance, to cause a copper deficiency, or to cause a myelopathy.

b. Epidemiological Evidence and Methodologies

"Epidemiologic evidence identifies agents that are associated with an increased risk of disease in groups of individuals, quantifies the amount of excess disease that is associated with an agent, and provides a profile of the type of individual who is likely to contract a disease after being exposed to an agent." Green, REFERENCE MANUAL 336. There are two classes of epidemiological evidence: analytical and descriptive. (*See* Lautenbach Rep. ¶ 42). Analytical evidence consists of experimental and observational studies, while descriptive evidence consists of case studies and case series. (*See id.*). The first type of analytical evidence, experimental studies, is discussed separately below. The second type, observational studies, includes case-control studies, cohort studies, cross-sectional studies, and ecological studies. (*See id.*); *see also* Green, REFERENCE MANUAL 339. Analytical studies, such as case-control studies and cohort studies, allow the investigator to determine the rates of disease in exposed and unexposed groups. *See* Green, REFERENCE MANUAL 338. This allows calculation of the increased risk of disease attributable to exposure to the agent. *See id.* 348.

Epidemiology is the "best evidence of causation in toxic tort cases." *Kilpatrick,* 613 F.3d at 1337 n. 8 (citation omitted); (*see also* Lautenbach Rep. ¶ 42 ("Analytic studies are most rigorous in identifying the determinants of a disease.")). Plaintiffs' experts have no analytical epidemiological evidence on which to base their inference of causation. [21] (*See* Lautenbach Rep. ¶ 20 ("[N]o analytic epidemiological studies exist to support or refute the association between Fixodent use and myeloneuropathy.")). Instead, Plaintiffs point to Dr. Lautenbach's testimony that analytical epidemiological evidence is not necessary to infer causation when one

has enough descriptive epidemiological evidence, like case studies, and a plausible biological explanation. (*See id.* ¶¶ 42–45).

21 Dr. Lautenbach:

Q. To the best of your knowledge, there are no controlled population-based epidemiologic studies testing whether there is an association between denture adhesive and the development of hematologic or neurologic disease. Correct?

A. That's correct.

(Lautenbach Dep. 28:19–25).

***6** The Eleventh Circuit, although it has not has not completely excluded the possibility that causation may be established by case studies, has been very hostile when experts have relied on them to infer causation. *See McClain,* 401 F.3d at 1254 ("[Case reports] may support other proof of causation.") Indeed, like Dr. Lautenbach, some have argued that "despite ... limitations, sometimes case reports can contribute to or be very good evidence of causation on their own." CARL F. CRANOR, TOXIC TORTS, SCIENCE, LAW, AND THE POSSIBILITY OF JUSTICE 116 (Cambridge 2006) [hereinafter CRANOR]. But "what makes case studies good evidence about causation is the analysis to which they are subjected and how scientists reason about them." *Id.* 115. Therefore, in the appropriate case, case studies may provide reliable evidence of causation. *But see Haggerty v. Upjohn Co.,* 950 F.Supp. 1160, 1165 (S.D.Fla.1996) ("[C]ase reports may provide anecdotal support, [but] they are no substitute for a scientifically designed and conducted inquiry.") (citing *Casey v. Ohio Medical Products,* 877 F.Supp. 1380, 1385 (N.D.Cal.1995)).

As discussed below, this is not an appropriate instance to rely on case studies because the case studies Plaintiffs' experts rely on suffer from a number of inaccuracies and methodological weaknesses that undermine their evidentiary value. There are also a number of problems with Plaintiffs' assertion that there is a plausible biological mechanism—Fixodent-induced copper-deficiency myelopathy; those weaknesses are also addressed below. Thus, while it is true Plaintiffs' experts, Dr. Lautenbach in particular, use a recognized epidemiological methodology, they have not done so with the degree of intellectual rigor characterized by practitioners in the field.

c. Background Risk of Disease

An important aspect of epidemiological reasoning is knowledge of background risk. Background risk of disease "is the risk a plaintiff and other members of the general public have of suffering the disease or injury that plaintiff alleges *without* exposure to the drug or chemical in question." *McClain,* 401 F.3d at 1243 (emphasis in original); *see also* Green, REFERENCE MANUAL 388. Because epidemiology aims to identify "agents that are associated with an increased risk of disease," Green, REFERENCE MANUAL at 336, one must know the background prevalence of a disease before one can determine if exposure to an agent has increased the risk of that disease. Thus, "[a] reliable methodolgy should take into account the background risk." *McClain,* 401 F.3d at 1243. Plaintiffs' causation experts uniformly testified that they did not know the background risk of copper-deficiency myelopathy.[22] This is a serious methodological deficiency,[23] which is evident in Dr. Landolph's reasoning:

22 Dr. Brewer:

Q. Do you know the incidence of myeloneuropathies in the United States?

A. No.

Q. Do you know the incidence of myeloneuropathies, myelopathies, or myeloneuropathies [sic] among uses of zinc-containing denture adhesives in the United States?

A. No.

Dr. Lautenbach:

Q. Do you know what the incidence of myelopathy is in the general population?

A. I don't. I'm not sure it's been well defined.

(Lautenbach Dep. 25:16–21).

Dr. Landolph:

Q. You are unable to give me a number setting forth the incidence of myeloneuropathy among users of zinc containing denture adhesives in the United states, correct?

A. That's correct, the precise number, I don't have that data.

(Landolph Dep. 11:14–19).

Dr. Greenberg:

Q. Do you know what the general incidence—excuse me. Do you know what the incidence of myelopathies is in the general population in the United States?

A. No.

Q. Do you know what the general incidence of myelopathy is in denture adhesive users in the United States?
A. No.
(Greenberg Dep. 28:7–15).

23 There is also nothing in the experts' reports or testimony about the background risk of hyperzincemia or copper deficiency.

Q. What is the incidence of myeloneuropathy in the general population in the United States? ....

*7 A. .... It seems to be not incredibly common. I don't know the exact number[, but] ... it seems to be sufficiently common, it being copper deficient myeloneuropathy among denture adhesive wearers that it's provoking the interest of the scientific and medical community to study at this further [. S]o the background is sufficiently low that when they are getting this now in addition to other causes they are beginning to identify that the sufferers, the patients have frequently used denture adhesives containing zinc, so the reports are becoming more frequent with time.

(Landolph Dep. 37:25–38:13).

This is not even good lay reasoning, much less reliable scientific reasoning.[24] Obviously, one cannot infer that denture cream increases the risk of a myelopathy merely from the scientific community's decision to study the question, and one cannot assume the authors of case reports know the background rate of the disease they are studying (especially here, when we have some of those scientists' testimony to the contrary). Moreover, the question of background risk is important because it could be coincidence that any particular denture-cream user has a myelopathy or copper-deficiency myelopathy. Some people use denture cream and some people have a myelopathy; it is possible (and depending on the incidence of myelopathies, likely) that some denture-cream users have an idiopathic myelopathy simply due to the background distribution of that disease. Without a baseline, any incidence may be coincidence. Accordingly, the absence of this data is a substantial weakness in Plaintiffs' experts' causal reasoning.

24 "The adjective 'scientific' implies a grounding in the methods and procedures of science. Similarly, the word 'knowledge' connotes more than subjective belief or unsupported speculation." *Daubert,* 509 U.S. at 590. "Proposed testimony must be supported by appropriate validation *i.e.*, 'good grounds,' based on what is known. In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Id.*

d. Understanding of the Physiological Processes Involved

"When [mechanistic evidence] is present it can greatly strengthen a causal inference, but when it is absent it does not necessarily undermine the inference." CRANOR 247; *see also* Green, REFERENCE MANUAL 378 ("When biological plausibility exists, it lends credence to an inference of causality."). Although Plaintiffs' experts are able to explain at least one[25] of the biological processes by which zinc interferes with copper absorption,[26] they acknowledge that "the mechanism by which hypocupremia leads to neurologic abnormalities in humans remains uncertain."[27] (Brewer Dep. 38:24–39:9). Moreover, there is no mechanistic evidence concerning the absorption of zinc from the Fixodent polymer, leaving its experimentally determined decreased bioavailablity unexplained. The Court acknowledges the mechanistic explanation of how zinc up-regulation of metallothenien leads to copper loss does lend some support the conclusion that Fixodent can block copper absorption. However, this supports only one premise in Plaintiffs' multi-step hypothesis; and the limited bio-availability of the zinc in Fixodent suggests this conclusion must be held tentatively.

25 Dr. Brewer:
Q. Okay. Now, are there various postulated mechanisms by which zinc might affect copper status?
A. Yes.
(Brewer Dep. 46:15–17).

26 Zinc causes an upregulation of metallothionein production in the enterocytes. Copper has a higher binding affinity for metallothionein than zinc. Thus, copper displaces zinc from metallothionein, remains in the enterocytes and is then lost in the stool as intestinal cells are sloughed off. Thus, there is a clear biological mechanism for excessive zinc ingestion causing copper deficiency.
(Lautenbach Rep. ¶ 15).

27 Dr. Brewer:

> Q. Going back to the zinc-induced copper deficiency syndrome that you referred to in your report, do you know if it has been scientifically established what the mechanism is whereby a deficiency in copper supposedly causes a myelopathy?
>
> A. No, I don't believe that there's a scientifically established mechanism.
>
> (Brewer Dep. 30:12–18; *see also* Greenberg Dep. 30:12–18).

e. Clinical Studies

The clinical trial, or randomized-trial, is a type of analytical epidemiological evidence, but this type of evidence is unlikely to be available in a toxic-tort case because it is unethical to randomly assign a human individual a potentially harmful dose of a suspected toxin. *See* Green, REFERENCE MANUAL 338 ("Ethical and practical constraints limit the use of such experimental methodologies to assessing the value of agents that are thought to be beneficial to human beings."). Courts do not demand and should not demand the results of a randomized, controlled study to prove causation in toxic-tort cases. Thus, the lack of a randomized, controlled experimental study showing that Fixodent causes copper-deficiency myelopathy does not undermine Plaintiffs' experts' inference of causation.[28] It should be noted that the record is not completely devoid of evidence from clinical trials: both Dr. Brewer's experiments to determine what dose of zinc acetate is necessary to place individuals into a negative copper balance and Procter & Gamble's pharmacokinetic studies are clinical-trial evidence. However, neither of these studies is dispositive of the ultimate question of whether Fixodent can cause copper-deficiency myelopathy.

28 However, as discussed, the lack of *any* analytic epidemiological studies does weaken Plaintiffs' experts' assertion of causation.

***8** While this ultimate question could not be subjected to a clinical study, it may be appropriate, practical, and ethical to conduct a clinical study to determine at what dose Fixodent may induce a negative copper balance. Such a study would bridge the gap between Dr. Brewer's copper-balance studies and Procter & Gamble's pharmacokinetic studies. It would not, however, allow one to infer the exposure to Fixodent required to induce the severe copper deficiency that Dr. Brewer testified would be necessary to produce neurological symptoms. (*See* Brewer Dep. 19:11–17 ("If I had to guess, I would say that you would have to have the copper down in the very low range for at least a few months before you develop the neurologic disease.")).

2. Plaintiffs' Experts' Data and Methodologies

Plaintiffs and their experts rely on several bases to support their inference of general causation: (1) a biologically plausible explanation, (2) case reports of denture-cream users who have neurological problems, (3) de-challenge evidence, (4) animal studies, and (5) an FDA notice.

a. Biologically Plausible Explanation

As discussed, a biologically plausible hypothesis can lend credence to a causal inference. Plaintiffs' experts hypothesize a multi-step causal chain linking the ingestion of Fixodent to a myelopathy. The experts rely on different types of evidence to support each premise in their hypothesis and then infer, based on their scientific judgment, that Fixodent can cause copper-deficiency myelopathy. The question before the Court is whether this ultimate inference is reliable. Making some of the implicit premises explicit,[29] Plaintiffs' hypothesis can be summarized as follows:

29 There are others which remain implicit such as assumptions about the amount of dietary copper consumed by denture wearers.

(1) Fixodent contains zinc.

(2) The zinc in Fixodent can be absorbed by the body.

(3) Absorption of enough zinc from any source can induce a negative copper balance.

(4) One can ingest enough zinc from Fixodent to place the body in a negative copper balance.

(5) Over time a zinc-induced negative copper balance can lead to a copper deficiency.

(6) A prolonged copper deficiency in humans can cause a myelopathy.

(7) Therefore, Fixodent can cause a myelopathy.

There are several reasons this hypothesis is not a basis from which to infer causation. First, as discussed,

Plaintiffs do not have any analytical epidemiological evidence showing that (4) is true; that is, that one can ingest enough Fixodent to induce a negative copper balance. Plaintiffs' experts also assume the truth of (5) without pointing to any analytical epidemiological evidence to show that it is true. Moreover, premise (6), that a copper deficiency can cause a myelopathy, is subject to ongoing scientific debate and is supported at present only by a few case reports.

Second, Plaintiffs' attorneys have treated this hypothesis like it is a deductive argument.[30] (*See* Brewer Opp'n 2 [ECF No. 1071] ("Defendants and their experts have chosen to ignore longaccepted, axiomatic scientific principles of zinc metabolism."); *see also id.* at 12 ("The case reports are not required to establish a causal link between the ingestion of excessive zinc and disease. That link has been known and understood for decades."); Hr'g Tr. at 93:20 ("There's no missing link.")). Although Plaintiffs' hypothesis resembles a deductive argument, it should not be confused for one. It is not the case that if, as Plaintiffs' attorneys claim, every premise is generally accepted by the scientific community, that the conclusion is accepted as well.

30 [I]nferences to conclusions are of two kinds: deductive and non-deductive. The defining feature of valid deductive inferences ... is that the conclusion is 'guaranteed' logically or semantically by the premises.... By contrast, nondeductive inferences are simply those whose conclusions are supported but not guaranteed by their premises. Even if the premises are true, the nondeductive link between premises and conclusions will have varying degrees of strength, unlike a deductive argument. In nondeductive arguments if the premises are true, they may offer much to little (or no) support for the conclusion in question. Moreover, the given premises will provide support for different possible conclusions .... CRANOR 129.

***9** In reality, Plaintiffs' argument is a type of inductive argument where some premises have a statistical component:

(1) Fixodent contains zinc.

(2) Excessive zinc ingestion, including from Fixodent, increases the risk of copper deficiency.

(3) Prolonged copper deficiency increases risk of a myelopathy.

(4) Therefore, Fixodent increases risk of a myelopathy.

As this makes apparent, general agreement on the truth of the premises would not guarantee Plaintiffs' conclusion is true.[31]

31 Consequently, the Court need not address whether zinc intake can cause copper deficiency (probably, in some people), or whether copper deficiency can cause myelopathy (maybe, in some people) because it would be unreliable for Plaintiffs' experts to infer from those premises—even if true—that Fixodent causes copper-deficiency myelopathy.

Third, in forming this hypothesis and concluding it supports causation, there is no indication Plaintiffs' experts or the authors of the articles tying denture cream to a myelopathy engaged in systematic scientific reasoning to conclude this hypothesis is the best explanation for what they observed in the case reports.[32] For instance, "in trying to understand causal relationships a researcher needs to consider a sufficiently complete list of plausible explanations to account for the evidence." CRANOR 130. Thus, before inferring Plaintiffs' hypothesis, that Fixodent causes a myelopathy is the best explanation for the neurological symptoms reported in the case reports, researchers should form a list of competing hypotheses. Those rival hypotheses should then be ranked "according to their plausibility based on the evidence available at the time." *Id.* at 131. Next, the researcher should "use the initial plausibility rankings to try to distinguish what other evidence might be available that would distinguish between the explanations—to separate more plausible from less plausible explanations—and seek it out." *Id.* Then all relevant evidence should be used to determine which hypothesis is the most likely. There is no evidence that Plaintiffs' experts or the case reports they rely on have been systematic in considering other plausible hypotheses[33] and excluding background risk. Plaintiffs' hypothesis, understood as a biological explanation, is not a reliable basis for their experts to conclude that Fixodent causes copper-deficiency myelopathy.[34]

32 The flaws in the methodologies of the case report articles, particularly the Hedera and Nations Articles, are discussed in detail below.

33 One interesting possibility is that denture wearers, particularly those using ill-fitting dentures, are more vulnerable to copper deficiency due to different eating habits caused by their dentures that lead to lower calorie intake and nutrient deficiencies. (Nelson Rep. 27–29 (citing NR Sahyoun *et al., The nutritional status of the older adult is associated with dentition status,* 103 J. AM. DIETET. ASSOC.. 61–66. (2003) [hereinafter Sahyoun 2003])). This might also raise interesting egg-shell plaintiff questions.

34 Dr. Landolph acknowledged that a hypothesis should be tested before concluding it is correct:

> Q. Once the hypothesis is generated, then from a scientific standpoint the hypothesis should be tested, correct?
>
> A. Yes, it should be tested experimentally, yes.
>
> (Landolph Dep. 28:11–21 [ECF No. 1144–1]).

Moreover, in verifying his hypothesis that zinc-acetate could control copper levels in Wilson's disease patients, Dr. Brewer "did a large number of copper balance studies and obtained results which confirmed [his] hypothesis." (Brewer Rep. 5 [ECF No. 1046–1]). This shows the level of intellectual rigor that has characterized Dr. Brewer's past work, but also highlights that he has not applied the same level of experimental rigor to confirm the link between Fixodent and copper-deficiency myelopathy. *See Kumho,* 526 U.S. at 152 ("The objective of [*Daubert's* gate-keeping requirement] .... is to make certain that an expert ... employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field."); *see also Kilpatrick,* 613 F.3d at 1336 (" 'Under the regime of *Daubert* ... a district judge asked to admit scientific evidence must determine whether the evidence is genuinely scientific, as distinct from being unscientific speculation offered by a genuine scientist.' ") (quoting *Allison v. McGhan Med. Corp.,* 184 F.3d 1300, 1316–17 (11th Cir.1999)).

b. Case Reports

Beyond their hypothesis itself, Plaintiffs' experts' conclusion that Fixodent can cause copper-deficiency myelopathy is almost entirely based on the information contained in a number of scientific articles reporting cases of patients who used denture creams who also had abnormal levels of zinc and copper in their blood and neurological symptoms.[35] The Court has carefully reviewed this literature, as well as other scientific literature the experts mention in their reports.

35 In addition to the Nations and Hedera Articles already cited, the other articles are: Hedera *et al., Myelopolyneuropathy and pancytopenia due to copper deficiency and high zinc levels of unknown origin,* 60 ARCH. NEUROL. . 1303 (2003) ("Hedera 2003"); Spinazzi *et al., Myelooptico-neuropathy in copper deficiency occurring after partial gastrectomy,* 254 NEUROL. 1012 (2007); Sibley *et al., Myelodysplasia and copper deficiency induced by denture paste,* 84 AM. J. OF HEMATOL. 612 (2009); Afrin, *Fatal copper deficiency from excessive use of zinc-based denture adhesive,* 340(2) AM. J. OF THE MED. SCIS. 164 (2010); Spain *et al., When metals compete: a case of copper deficiency myeloneuropathy and anemia,* 5(2) NAT'L CLIN. PRAC. NEUROL. . 106 (2009).

"Causal attribution based on case studies must be regarded with caution." Green, REFERENCE MANUAL 475. Courts in the Eleventh Circuit have been particularly unwelcoming to experts who infer causation from case reports. *See, e.g., Hendrix,* 609 F.3d at 1197 (finding case reports by themselves are "insufficient to show general causation"); *McClain,* 401 F.3d at 1254 ("[C]ase reports raise questions; they do not answer them."); *Rider,* 295 F.3d at 1199 (holding "case reports alone ordinarily cannot prove causation"); *Haggerty,* 950 F.Supp. at 1165 ("[W]hile case reports may provide anecdotal support, they are no substitute for a scientifically designed and conducted inquiry."). Nevertheless, the Eleventh Circuit has not foreclosed using case reports as supporting an inference of causation when accompanied by other proof of causation.[36] *See McClain,* 401 F.3d at 1254.

36 The only scientific literature supporting a link between copper deficiency and a myelopathy is contained in case reports and animal studies. A subset of those case reports links excessive zinc ingestion to copper-deficiency myelopathy. The Court focuses on this last set of case reports because those would provide the only direct support that Fixodent could cause a myelopathy. Recall from above, even if those intermediate premises were true, one could not reliably infer the conclusion that Fixodent causes myelopathy.

***10** In addition to it being unreliable, as a general matter, to rely on case reports to infer general causation, there are a number of particular problems with the case reports relied on by Plaintiffs' experts in this case. The report prepared by Procter & Gamble's expert, Dr. Lorene Nelson[37] (the "Nelson Report" [ECF No. 1046–12]), was extremely helpful to the Court in identifying the factual inaccuracies and methodological weaknesses[38] in the articles on which Plaintiffs' experts rely.

37 Dr. Nelson studies the environmental causes of nervous system disorders and leads a large research program to identify environmental risk factors and susceptibility genes for neurodegenerative diseases. (*See* Nelson Rep. 4).

38 Dr. Nelson observes that the case studies on which Plaintiffs' causation experts rely suffer from flaws such as incomplete data ascertainment, poor quality of exposure measurement, inconsistent case definition, and other sources of bias, and therefore provide even less support for the hypothesized causal association. (Nelson Rep. 9).

Dr. Nelson did an independent review of all of the literature concerning the link between zinc-containing denture cream and increased risk of a myelopathy. The total number of unduplicated cases she found in the literature was 21. Within those 21 cases, ten patients reported using only Poligrip, four reported using both Poligrip and Fixodent, and one reported using Fixodent exclusively; the type of denture cream used in the remaining seven cases was not reported.[39] (*See* Nelson Rep. 12–13).

39 As discussed, the zinc in Fixodent is bio-available, but the pharmacokinetic studies show that its inclusion in the Fixodent polymer reduces its absorption as compared with more soluble forms of zinc. (*See* PK Study 35). Poligrip uses a different polymer, for which pharmacokinetic information is not available in this litigation, and contains twice the amount of zinc as Fixodent. These differences severely limit the conclusions that can be drawn from the cases where patients used Poligrip. Fixodent is not Poligrip, and neither is a tube of zinc. *See McClain,* 401 F.3d at 1246 (" '[E]ven minor deviations in chemical structure can radically change a particular substance's properties and propensities.' ") (citation omitted).

Dr. Nelson also observes that copper-deficiency myelopathy lacks widely accepted or published case definition criteria identifying its clinical features, imaging abnormalities, and clinical disease course. (*See id.* at 10). In Response, Plaintiffs argue there is a clear phenotype of patients who have zinc-induced copper-deficiency myelopathy and point to Dr. Greenberg's deposition testimony. (*See* Greenberg Dep. at 71:20–72:22 April 29, 2011 [ECF No. 1072–1]). However, Dr. Greenberg did not select the individuals in the case reports; the authors of those reports did, and what matters is what they thought the scope of the disease was. That is, the case reports may not have used Dr. Greenberg's definition of copper-deficiency myelopathy.

There are very good reasons to believe the cases reported in the literature suggesting an association between denture cream and neurological symptoms included people who were not suffering from copper-deficiency myelopathy. First, there is not a well-established clinical presentation for copper-deficiency myelopathy. Dr. Kumar, the author of some of the studies on which Plaintiffs' experts rely and who is cited by all of the case reports linking denture cream to a myelopathy, has written extensively on the clinical features of copper-deficiency myeloneuropathy. (*See* Nelson Rep. 10–11 (citing numerous articles by Kumar)). Dr. Kumar acknowledges that copper-deficiency myelopathy does not have a specific diagnosis code within the international classification of disease coding system. (*See id.* at 10 (citing Kumar *et al., Copper deficiency myeloneuropathy,* Medlink Neurology (Nov. 22, 2010), www.medlink.com (last visited June 13, 2011) [hereinafter Kumar 2010])). Second, in a recent article, Dr. Kumar specifically notes that some of the cases in the Nations Article would require additional study before they were classified as copper-deficiency myeloneuropathy. (*See id.* (citing Kumar 2010)). Moreover, a recent article surveying the literature on copper-deficiency myelopathy reached the same conclusion as Dr. Kumar and found that some of the conditions reported in the case reports may be "less clearly causally related to copper deficiency." (Nelson Rep. 10–11 (citing S.R. Jaiser *et al., Copper Deficiency Myelopathy,* J. NEUROL. 1 (Published Online 2010))).

***11** Third, Dr. Boyer, one of the authors of the Nations Article, testified "the patients in our study had more of a neuropathy than a myelopathy, so involving the peripheral nerve rather than the spinal cord" (Boyer Dep.

32:10–14), which directly contradicts Dr. Greenberg's description of Ms. Chapman's condition (*see* Greenberg Dep. 87:15–17 ("She doesn't have a peripheral neuropathy .")). These inconsistencies in case definition limit the evidentiary value of the case reports to support an inference of causation because it is not even clear all of the case subjects had copper-deficiency myelopathy.[40] *See* Green, REFERENCE MANUAL 379 ("A study that finds that an agent is associated with many different diseases should be examined skeptically.").

40 As Dr. Nelson points out and the Court agrees, "there is considerable variability in the constellation of features that are presented for the patients that are presented for the subjects of the various anecdotal reports." (Nelson Rep. 11 (citing Nations and Hedera Articles)).

Dr. Nelson also notes that the Nations and Hedera Articles suffer from a number of methodological weaknesses that could introduce bias. First, it is not clear that the articles thoroughly excluded other sources of zinc to which the patients may have been exposed; neither the Nations or Hedera Article includes a description of the specific methods used to question patients about possible zinc exposure. In the absence of a standard set of questions for collecting exposure information it is likely that each patient underwent different questions administered in an openended format that may have biased the patients' responses.[41] Under those circumstances, it is possible that the patients were aware the studies were investigating the hypothesis that zinc-containing denture creams could be responsible for their condition.[42] This knowledge could have affected the subjects' answers during the interviews for the study.

41 Dr. Brewer:

Q. ... Was there a written questionnaire of any type that was to be utilized with regard to the patients that were contacted?

A. I assume you're referring to the questionnaire regarding dental adhesive, and not that I'm aware of. I think that after we became aware of the Nations article, then it was pretty obvious that you had to ask do you have ill-fitting dentures, do you use dental adhesives, and do you use—and what is its name and do you use a large amount of it, how much do you use. But those, that's an informal set of questions that the various investigators were asking these patients.

Q. And the various investigators were free to ask those questions in any manner which they personally felt appropriate?

A. Yes.

(Brewer Dep. 57:1–17).

42 The case reports also do not consider the possibility of confounding bias. For instance, as discussed, at least one analytical study suggests that denture wearers, particularly those using ill-fitting dentures, have lower calorie intake and lower levels of several nutrients than dentate people. (Nelson Rep. 27–29 (citing Sahyoun 2003)).

There are also some specific reasons Plaintiffs' experts cannot rely on the Nations Report to support an inference of causation. The Nations Article phrases its conclusions tentatively, explaining:

> We speculate that the copper deficiency in these four patients was secondary to ingestion of denture cream .... These findings, while not proving a causal relationship, warrant routine inquiry about the use of denture cream, in addition to zinc supplements, during the clinical evaluation of patients with myeloneuropathy and hematologic dysfunction.

(Nations Article 642). While it is common in scientific literature for investigators to couch their conclusions litotically, *see* CRANOR 192–197 ("Scientists tend to hedge their claims in scientific papers"), the conclusion of the Nations Article seems to the Court to be a sincere expression of uncertainty.[43] Because the authors of the Nations Article themselves do not conclude there is a causal relationship between the use of Fixodent and neurological symptoms, it is inappropriate for Plaintiffs' experts to draw that conclusion for them. *McClain,* 401 F.3d at 1248 (decrying "unauthorized conclusions from limited data—conclusions the authors of the study d[id] not make"); *In re Accutane Prods. Liab.,* No. 1626, 2009 WL 2496444, at *2 (M.D.Fla. Aug. 11, 2009) ("[W]hen an expert relies on the studies of others, he must not exceed the limitations the authors themselves place on the study."). Additionally, while the Nations Article states that all of the subjects' copper levels returned to normal after they stopped using denture cream, at least one patient continued to have depressed copper even with

copper supplementation. (*See* Boyer Dep. 239:1–240:15). Finally, none of the subjects in the Nations Article reported having used Fixodent.

43 Indeed, Dr. Philip Boyer, who is one of the authors of the Nations Article, testified that a case-control or cohort study "would be a perfect thing to do. And as I mentioned, I proposed that to the dental faculty here as a study that would be good to do, but [it] has not been done." (Boyer Dep. 331:2–12).

***12** The Hedera Article, which was co-authored by Dr. Brewer, also suffers from its own particular deficiencies.[44] First, there are methodological problems. In their deposition testimony, Drs. Hedera and Brewer acknowledged they did not establish a case definition or set of diagnostic criteria (*see* Brewer Dep. 34:7–24), they followed no written protocol (*see id.* 35:4–7, 56:6–25, 57:1–17), and they did not know how much denture cream the patients used (*see* Hedera Dep. 261:19–262:20, 263:4–9) or how long the patients had used denture cream (*see id.* 253:10–24). They also did not take the subjects' complete medical histories to exclude potential alternative causes for their neurological symptoms. (*See id.* 74:9–76:5, 79:2–80:6).[45]

44 In her report, Dr. Nelson questioned whether the Hedera Article had undergone full peer review based on the rapidity with which the article moved from acceptance to publication. (*See* Nelson Rep. 17).

45 The Hedera Article also estimates the bio-availability of the zinc in Fixodent. (*See* Hedera Article 2, 4). The pharmacokinetic studies suggest the estimate is much too high.

Second, Dr. Brewer acknowledged in his deposition that there were inaccuracies in the Hedera Article. (Brewer Dep. 128:18–23 ("Q. So when the article says that their copper and zinc normalized after stopping denture cream, that's not an accurate statement, is it? A. It's got some inaccuracy to it .... It's somewhat inaccurate.)). Dr. Hedera also acknowledged that some patients in his article were inaccurately described as having abnormal blood zinc and copper levels when their lab results were actually within the normal range. (*See* Hedera Dep. 277:8–14; 293:8–18; 297:7–10).

Some of these inaccuracies are very significant. The Article mischaracterizes the results to make it appear that all the patients' blood zinc and copper levels returned to the normal range[46] when the patients stopped using denture cream. (*See* Hedera Article Abstract). In fact, even after cessation of denture cream, seven of eight patients still had high urine zinc and six of eleven continued to have high plasma zinc. (*See* Brewer Dep. 127:25–129:14). In Dr. Brewer's expert report, in discussing the Hedera Article he states, "in this series of eleven patients the cessation of the use of the denture adhesives led to the normalization of zinc levels. In all eleven patients only the use of zinc containing denture adhesives could explain the clinical manifestations." (Brewer Rep. 8 [ECF No. 1046–1]). Dr. Brewer's conclusion is not reliable because it is based on an inaccurate factual premise.

46 The subjects were given copper supplements when they were taken off denture cream. (*See* Hedera Article 2). Therefore, it is not clear whether it was the cessation of denture-cream use or copper supplementation that raised the subjects' blood copper levels. This particular confounding bias afflicts a number of the case-report articles.

Third, as mentioned, there is only one patient in all of the case reports who is described as having used Fixodent exclusively. That patient is documented in the Hedera Article as patient # 2. (*See* Hedera Article 3). The case report does not identify how much Fixodent that patient used, but only states he, along with the other subjects, "reported applying large amounts of the denture creams." (*Id.* at 2). This single Fixodent user had near-normal zinc levels before stopping use of the product, and his copper level remained abnormally low after cessation; he also had "Axonal Polyneuropathy" rather than "Demyelinization." (*Id.* at 3). Case reports suggesting a link between denture cream and "axonal polyneuropathy" cannot act as reliable evidence of an association between Fixodent use and a *myelopathy. See McClain,* 401 F.3d at 1246 ("Evidence suggest[ing] that [a chemical] may cause ischemic stroke does not apply to situations involving hemorrhagic stroke. This is 'a leap of faith'....") (quoting *Rider,* 295 F.3d at 1202).

***13** The Court has also considered the other case report articles suggesting a link between zinccontaining denture cream and finds they suffer from their own methodological flaws. In particular, none specifies the subjects used Fixodent. Accordingly, an inference of causation based on this collection of case reports would be unreliable. *See* Ralph R Cook, *Epidemiology for Toxicologists* in PRINCIPLES AND METHODS OF

TOXICOLOGY 559 (A. Wallace Hayes 5th ed., 2008) ("Although the theories derived from case studies are not always wrong, history teaches that they are seldom right.").

c. De-challenge Data

"When ... eliminating exposure reduces the incidence of disease, this factor strongly supports causal relationship." Green, REFERENCE MANUAL 378. According to Plaintiffs, their experts cite the Nations and Hedera Articles "specifically to demonstrate that upon de-challenge with Fixodent, the patients in the studies saw their zinc levels normalize in short order and we[re] able to normalize copper levels to the point where supplementation could be stopped in each." (Resp to Supp. Brewer Br. 19 [ECF No. 1167]). However, as a careful review of the Nations and Hedera Articles has just shown, only one of those patients exclusively used Fixodent, and many of the patients continued to have abnormal levels of zinc and copper in their blood and urine. Additionally, cessation of denture cream use was only sometimes followed by any neurological improvement by the patients in those articles. Accordingly, the de-challenge data does not reliably show that cessation of Fixodent leads to amelioration of the symptoms of copper-deficiency.

d. Animal Studies

Although some animal studies are mentioned in passing in Plaintiffs' experts' reports, no expert explicitly relies on them in forming his opinions. *See Allison v. McGhan Med. Corp.,* 184 F.3d 1300, 1314 (11th Cir.1999) (citing *In re Paoli R.R. Yard PCB Litig.,* 35 F.3d 717, 743 (3d Cir.1994 ("[I]n order for animal studies to be admissible to prove causation in humans, there must be good grounds to extrapolate from animals to humans.")). Because Plaintiffs' experts do not even attempt to argue the animal studies can be extrapolated to humans, the Court will not make the argument for them. It will however, pause to note that swayback, a neurological disease caused in second-generation sheep whose mothers grazed in copper-deficient pastureland, provides little support for the claim that zinc-induced copper deficiency in humans leads to a myelopathy. *See* Bennetts, *et al., Copper Deficiency in Sheep in Western Australia: A Preliminary Account of the Aetiology of Enzootic Ataxia of Lambs and an Anaemia of Ewes,* 13 AUST. VET.. J. 138 (1937); *see also* Van Campen, *Zinc Interference with Copper Absorption in Rats;* 91 J. NUTR. 473 (1967) ([ECF No. 1072–6]). Moreover, at most these studies could supply support for some of the premises of Plaintiffs' hypothesis; as explained, one cannot infer causation from a hypothesis.

e. The Food and Drug Administration ("FDA") Notice

***14** Dr. Lautenbach observes "[i]n response to the increasing adverse event reports, the FDA noted 'there are literature and research that suggest that zinc contained in some denture adhesives may be a contributing factor in these adverse events.' " (Lautenbach Rep. ¶ 40 (citing FDA Notice and Recommended Action—2/23/11)). In his view the FDA's action shows the agency has acknowledged "a compelling signal for an association between Fixodent and myeloneuropathy." (*Id.* at ¶ 41). There are three problems with this argument. First, the FDA only recognizes an association, and "showing association is far removed from proving *causation." Allison,* 184 F.3d at 1315 n. 16 (emphasis in original). Second, like in *McClain,* where the Eleventh Circuit found a more strident FDA warning not to be a sound basis for an inference of causation, the FDA Notice "relie[s] heavily on adverse event reports without sufficient controls." 401 F.3d at 1248. Third, regulatory agencies follow different standards than courts in toxic-tort cases. "The risk—utility analysis involves a much lower standard than that which is demanded by a court of law. A regulatory agency such as the FDA may choose to err on the side of caution. Courts, however, are required under the *Daubert* trilogy to engage in an objective review of evidence to determine whether it has sufficient basis to be considered reliable." *McClain,* 401 F.3d at 1250. Accordingly, Plaintiffs' experts may not establish causation by reliance on the FDA Notice.

B. Specific Causation: Whether Dr. Greenberg Used a Reliable Scientific Methodology to Conclude Fixodent Caused Ms. Chapman's Illness.

Dr. Greenberg would testify that Ms. Chapman suffers from zinc-induced copper-deficiency myelopathy caused by her use of Fixodent. (*See* Greenberg Rep. 10–11 ("[A] diagnosis of copper deficiency myelopathy is certain ... [and] in this patient, it was precisely the ingested zinc in the denture cream that caused her copper deficiency.")). To reach this conclusion, Dr. Greenberg performed a differential diagnosis.

A differential diagnosis or differential etiology " 'is a standard scientific technique of identifying the cause of a medical problem by eliminating the likely causes until the most probable one is isolated.' " *Kilpatrick,* 613 F.3d at 1336 n. 7 (quoting *Westberry v. Gislaved Gummi,* 178 F.3d 257, 262 (4th Cir.1999)); *see also McClain,* 401 F.3d at 1252 (internal citation omitted) ("[A differential diagnosis is] the determination of which one of two or more diseases or conditions a patient is suffering from, by systematically comparing and contrasting their clinical findings."). In *Hendrix,* the Eleventh Circuit laid out the reliable procedure for conducting a differential diagnosis. The doctor must begin with a comprehensive list of potential causes, and then engage in "a medical process of elimination whereby all possible causes of the condition are considered and ruled out one-by-one, leaving only one cause remaining." *Hendrix,* 609 F.3d at 1195.

***15** To begin, although permitted in some circuits, the Eleventh Circuit does not allow general causation to be proved by a differential diagnosis. *Compare McClain,* 401 F.3d at 1253 ("In the absence of [a showing of general causation] ... a differential diagnosis generally may not serve as a reliable basis for an expert opinion on causation in a toxic tort case."), *with Westberry,* 178 F.3d at 266 (4th Cir.) ("A reliable differential diagnosis provides a valid basis for an expert opinion on [general] causation."). This means "the district court must ensure that, for each possible cause the expert 'rules in' at the first stage of the analysis, the expert's opinion on general causation is 'derived from scientifically valid methodology.' " *Hendrix,* 609 F.3d at 1195 (quoting *Hollander v. Sandoz Pharm. Corp.,* 289 F.3d 1193, 1211 (10th Cir.2002)). Recall that Dr. Greenberg's conclusion that denture cream can cause copper-deficiency myelopathy is based on the same case reports that Drs. Brewer, Landolph, and Lautenbach cite. (*See* Greenberg Rep. 1 ("Between 2007–2009, several publications established that zinc poisoning from certain denture adhesive creams are the most common cause of copper deficiency myelopathy.") (citing case reports including the Nations and Hedera Articles)).[47] Without a reliable basis to infer Fixodent causes copper-deficiency myelopathy, a differential diagnosis reaching that conclusion is, in effect, a detailed, unpublished case report. As discussed, case reports can support other evidence of general causation but are not reliable bases to infer general causation. Accordingly, Dr. Greenberg's differential diagnosis is not reliable as a matter of law in the Eleventh Circuit because he ruled-in and considered an etiology—Fixodent-induced copper-deficiency myelopathy—that has not been established to cause Ms. Chapman's disease.[48]

47 Dr. Greenberg also fails to consider that Fixodent is not 100 percent bio-available, as suggested by the pharmacokinetic studies. (*See* Greenberg Rep. 3).

48 Plaintiffs make much of the fact that some of Defendant's experts acknowledge that a copper-deficiency myelopathy should be part of the differential diagnosis of Ms. Chapman. The Court has not decided whether there is such a thing as copper-deficiency myelopathy, it only decides there is no reliable basis on which Plaintiffs' experts may conclude there is such a thing as Fixodent-induced copper-deficiency myelopathy. The existence of copper-deficiency myelopathy is only one premise of Plaintiffs' hypothesis.

A second problem with Dr. Greenberg's differential diagnosis is that he did not rule-in all possible causes before he started ruling things out. The report itself contains a section titled "Consideration of alternative diagnoses" where Dr. Greenberg lists, in addition to copper-deficiency, three other potential causes of Ms. Chapman's neurological syndrome: structural spinal cord injury, multiple sclerosis, and vitamin B12 deficiency. (*See* Greenberg Rep. 2–3). For Ms. Chapman's hematological syndrome, Dr. Greenberg ruled in lymphoproliferative disorders. (*See id.*). He also considered malabsorption and gastric bypass surgery as potential causes for her copper-deficiency. (*See id.*).

Defendants contend this list is much too short and that Dr. Greenberg should have also considered a "long list of hereditary and acquired diseases that could potentially cause Plaintiff Chapman's myelopathy" including "adrenomyeloneuropathy, complicated hereditary spastic paraplegia, ... Charcot–Marie–Tooth disease ..., hereditary motor and sensory neuropathy Type V, subtypes of spinocerebeller atrophy, ... hereditary ataxia with neuropathy .... vitamin E deficiency, Sjogren's syndrome, sarcoidosis, HTLV–1, neuromylitis optica, and a multiple vitamin deficiency syndrome." (Brewer Mot. at 18 n. 21). Defendants point out that "hereditary neuropathies, which include myelopathies, are far more common than copper-deficiency myelopathies," and thus Ms. Chapman's myelopathy is "more likely caused by a genetic condition than by Fixodent," especially

considering her personal medical history. (Brewer Reply 9 [ECF No. 1089]).

***16** According to Plaintiffs, Dr. Greenberg did consider all of these "and then moved on to consider the more likely alternatives until conclusively determining that Ms. Chapman suffered from [copper-deficiency myelopathy] and blood dyscrasias caused by zinc induced copper deficiency." (Brewer Opp'n 18). In his deposition, Dr. Greenberg testified:

> The differential diagnosis for a myelopathy of this particular nature, one that involves prominent dorsal column involvement, and also has this lower motor neuron degeneration, is extremely limited. It's copper deficiency and B12 deficiency. I really don't think other things are reasonable. One can always expand a differential diagnosis, *and we often do to be cautious and to not make mistakes,* but to have a reasonable differential, those are the ones.
>
> If one then throws in the hematological picture, an uncommon hematological picture that she's developed of anemia [and] neutropenia that baffled her doctors who saw her, including a hematologist, who stated that he did not feel this was due to B12 deficiency, then we're just left with copper deficiency.

(Greenberg Dep. 86:11–20).

Notably, Dr. Greenberg says "to be cautious and to not make mistakes," "[we often] expand a differential diagnosis" (*id.* 86:17–19), but acknowledges he did not do so here. This suggests that Dr. Greenberg did not employ "the same level of rigor that characterizes the practice of an expert in the relevant field" in reaching the diagnosis of Ms. Chapman. *Daubert,* 526 U.S. at 152. This is confirmed by Dr. Greenberg's decision to perform "a reasonable test" to address "the possibility of an ... arterial venous malformation, in the thoracic spinal cord" after he wrote his report. (Greenberg Dep. 16:5–17:7). His failure to perform a test he considered reasonable before opining on the cause of Ms. Chapman's disease shows a lack of methodological rigor in reaching the diagnosis in his report. Dr. Greenberg also did not consider the possibility of an idiopathic cause for Ms. Chapman's myelopathy. *See Kilpatrick,* 613 F.3d at 1342 ("The failure to take into account the potential for idiopathically occurring [disease]—particularly when [the disease] is a relatively new phenomenon in need of further study—placed the reliability of [the Doctor's] conclusions in further doubt.").

For these reasons, Dr. Greenberg did not perform a reliable differential diagnosis in reaching the conclusion that Ms. Chapman suffers from zinc-induced copper-deficiency myelopathy. *Daubert* requires Dr. Greenberg's testimony on specific causation be excluded.

C. Testimony of Drs. Wogalter, Von Fraunhofer, and Raffa

Because the Court finds that no expert will be permitted to testify to general or specific causation, the testimony of Drs. Wogalter and Von Fraunhofer, who assume the toxicity of Fixodent as a predicate for their testimony, is likely no longer relevant. The same is true for Dr. Raffa's proposed testimony on Procter & Gamble's assets, which would be relevant to a punitive damages claim. Therefore, the Court will grant the Motions seeking to preclude these experts from testifying on relevancy grounds.

IV. CONCLUSION

***17** Plaintiffs have put forth a superficially appealing hypothesis that prolonged use of very large amounts of Fixodent may cause copper-deficiency. Plaintiffs' experts have based their conclusions on a modest amount of animal studies, mechanistic processes, epidemiological studies, and case studies indicating elemental zinc in an unknown dose amount may cause a copper deficiency, which, if allowed to persist for an unknown time, may cause nervous system problems in some individuals. From this information, they induce that the zinc contained in the polymer in Fixodent can be absorbed in significant enough quantities to form the first link in the causal chain —the unknown dose of zinc.

This theory is not ridiculous, but neither is it necessarily true; it is ripe for testing. In short, taking everything together, there is enough data in the scientific literature to *hypothesize* causation, but not to *infer* it. Hypotheses are verified by testing, not by submitting them to lay juries for a vote. It may very well be that Fixodent in extremely large doses over many years can cause copper deficiency and neurological problems, but the methodology Plaintiffs' experts have used in reaching that conclusion will not reliably produce correct determinations of causation. In

a toxic torts case, more reliable evidence is required. Accordingly, it is

ORDERED AND ADJUDGED as follows:

1. The Motion to Exclude the Opinions of Plaintiffs' Experts Drs .5 Brewer, Greenberg, and Landolph **[ECF No. 1040]** is **GRANTED.**

2. The remaining *Daubert* motions **[ECF Nos. 1041–1044]** are, of necessity, **GRANTED.**

DONE AND ORDERED.

(Brewer Dep. 73:2–9).

All Citations

Not Reported in F.Supp.2d, 2011 WL 9375632, Prod.Liab.Rep. (CCH) P 18,924

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Exhibit P

2012 WL 12337860
Only the Westlaw citation is currently available.
United States District Court,
D. Utah,
Central Division.

Toshiko OKUDA, Plaintiff,
v.
WYETH, et al., Defendants.

No. 1:04–cv–80 DN.
|
Signed July 24, 2012.

Attorneys and Law Firms

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ORDER ON DEFDENDANTS' MOTIONS IN LIMINE

DAVID NUFFER, District Judge.

***1** After careful review of the memoranda and other materials submitted by the parties, the Court rules on Defendants' motions in limine as follows:

IT IS HEREBY ORDERED that Defendants' motion in limine no. 1 (docket no. 178) to exclude argument regarding punitive damages is GRANTED. Under Utah Code Ann. § 78B–8–203:

> (1) Punitive damages may not be awarded if a drug causing the claimant's harm:
>
> > (a) received premarket approval or licensure by the Federal Food and Drug Administration under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. Section 301 et seq. or the Public Health Service Act, 42 U.S.C. Section 201 et seq....

The requirements of this statute are disjunctive, so that subparagraph (1)(b), applicable to over-the-counter medications, is not applicable.[1] The statute makes no exception to its application based on the relative time of use and approval or based on off-label use or concurrent use with other approved drugs. The issue of preemption does not arise because Plaintiff has produced no evidence that Defendants withheld or misrepresented information Defendants were required to submit to the FDA. In light of this ruling, Plaintiff shall not characterize Defendants' actions as malicious or reprehensible or argue (or imply) that the jury should punish Defendants by an award of damages.

1 *Compare* Ohio Rev.Code Ann. § 2307.80(C)(1); Or.Rev.Stat. Ann. § 30.927; and N.J. Stat. Ann. § 2A:58C–5.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 2 (docket no. 233) to exclude evidence and argument regarding the number of women whose breast cancers were purportedly caused by hormone therapy is DENIED. This evidence is relevant to the issue of general causation, as well as the need for further testing, the adequacy of the warnings given, and the risk/benefit analysis. Weaknesses in the studies giving rise to these numbers may be established on cross-examination or by Defendants' experts.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 3 (docket no. 235) to exclude marketing evidence on which neither Plaintiff nor her physicians relied is GRANTED. Plaintiff has thus far failed to present evidence that she or her physicians relied on specific marketing materials. They are not admissible as circumstantial evidence of the source of any belief of Plaintiff or her physicians in off-label benefits, because that connection is too speculative and the marketing

evidence will confuse the jury and needlessly consume time.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 4 (docket no. 237) to exclude evidence of medical articles purportedly "ghostwritten" by professional writers acting on Wyeth's behalf is GRANTED. Plaintiff has not produced sufficient evidence that she or her prescribing physicians relied on any ghostwritten article in taking or prescribing the HRT drugs at issue or that the information in the articles is false. The fact that Wyeth was engaging in a fairly common, but little known practice, with a pejorative name would distract the jury and needlessly consume time. Plaintiff relies on the articles to show that Defendants were actively engaged in a campaign to overemphasize the benefits and downplay the breast cancer risks. However, the overpromotion theory only comes into play if the warnings given were adequate *and* the prescribing physicians disregarded the warnings in reliance on the promotional materials.

*2 IT IS FURTHER ORDERED that Defendants' motion in limine no. 5 (docket no. 239) to exclude causality assessments made by clinical investigators when medical study participants report an adverse medical event in the course of the study is GRANTED IN PART AND DENIED IN PART. The causality assessments are relevant to the issue of Defendants' knowledge of the association between their HRT drugs and breast cancer. To that extent, the motion is denied. However, the evidence is not admissible to rebut the contention by Defendants' experts that it is not scientifically possible to determine the cause of breast cancer with respect to a particular patient. Similarly, the evidence may not be used to argue that Wyeth's causality assessments are similar to, or otherwise demonstrate support for, the causation analysis offered by Plaintiff's experts. The causality assessments are clearly not a scientifically reliable means to determine the cause of cancer and will not be admitted for this purpose. For this same reason, the results of any such causality assessment will not be admitted. Accordingly, except as outlined above, the motion is granted.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 6 (docket no. 241) to exclude warnings and labeling changes that post-date Plaintiff's use of hormone therapy medications is DENIED. These labels may be used to establish proximate cause on the issue of the adequacy of the warnings: that adequate study would have resulted in stronger warnings and such warnings would have changed the plaintiff's physicians' prescribing practices. Plaintiff intends to establish that her physicians would have and actually did alter their prescription practices in the face of these warnings. The new warnings and labels are not subsequent remedial measures under Fed.R.Evid. 407 because they were required by the FDA.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 7 (docket no. 243) to exclude any evidence or testimony regarding testing that could have been done to further investigate the potential link between Defendants' hormone therapy ("HT") medications and breast cancer risk is DENIED. This order is consistent with the order entered July 6, 2012 (docket no. 231). Also consistent with that order, opinion evidence purporting to set or identify an objective standard for testing that Defendants should have performed will not be permitted. A curative instruction may be appropriate to clarify the lack of an objective standard for testing.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 8 (docket no. 245) to exclude at trial evidence and argument regarding Defendants' sales representatives' who did not call on or influence Plaintiff's prescribers during the relevant time period, *i.e.*, when Plaintiff was taking Defendants' estrogen and progestin (E+P) drugs, is GRANTED.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 9 (docket no. 247) to exclude evidence of the relationship between Premarin and endometrial cancer is GRANTED IN PART AND DENIED IN PART. While it may be that, as Plaintiff claims, "[h]ormones cause hormone-receptor positive cancers by promoting the growth of existing hormone-dependent abnormalities into full-blown, clinical cancer," [2] evidence of the relationship between Premarin and endometrial cancer has the potential for confusion and prejudice. The court is alerted to this issue, and shall ensure that Plaintiff limits presentation of and emphasis on such evidence. Plaintiff may not argue that because Premarin was linked to endometrial cancer, then E & P HT causes breast cancer, or that Defendants' response to the endometrial cancer issue in 1975 means they must have been aware of and hiding the breast cancer risk of E & P HT. Evidence of the 1975 conflict between the FDA and Wyeth

over the marketing response to the Premarin-endometrial cancer link appears to violate Rule 404. If Defendants argue that when FDA standards are met they have no additional duties, Plaintiff may present evidence of Defendants' response to the discovery of the endometrial cancer/estrogen association and the FDA's response to Defendants.

2 Plaintiff's Opposition to Defendants' Motion in Limine No. 9 ... at 3, docket no. 289, filed July 16, 2012.

*3 IT IS FURTHER ORDERED that Defendants' motion in limine no. 10 (docket no. 249) to exclude evidence and testimony regarding prescription data collected by IMS Health Inc. is DENIED. According to Defendants:

> IMS collects and analyzes pharmaceutical prescription data, then sells the results to the pharmaceutical industry, which uses the information for marketing and other business purposes. IMS purchases data on filled prescriptions (stripped of information that would identify patients) from approximately 70 percent of United States pharmacies. [3]

3 Defendants' Memorandum in Support of their Motion in Limine No. 10 ... at 2, docket no. 250, filed July 6, 2012.

This information may be helpful to show that prescribers changed their prescription issuance after the WHI study results became available in 2002. However, Plaintiff has not demonstrated foundation for admission of the IMS data, so admissibility is not determined. HT use and incidence of breast cancer before and after the WHI report have been regarded as related and are thus relevant to the issue of causation.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 11 (docket no. 251) to exclude reference to and evidence of Defendants' wealth, profit margins for hormone therapy and/or alleged "profit motive" is GRANTED. Defendants' wealth has no relevance to this case, except to the extent Defendants might argue that they were financially unable to complete any necessary testing. Defendants have given no indication that they intend to do so. Defendants' motives are not central to this case.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 12 (docket no. 253) to preclude Plaintiff from making any reference to the absence of a corporate representative for Defendants at trial is DENIED. The presence or absence of a corporate representative (or a fact witness) is not evidence but is a fact of the procedure of trial. It may be argued, and counter-argument may be made.

IT IS FURTHER ORDERED that Defendants motion in limine no. 13 (docket no. 255) to exclude improper and prejudicial statements and argument is DENIED. The parties are, however, reminded that the trial order contains specific instructions regarding courtroom behavior and that:

- Opening statements are *statements* and not argument;
- Brief opening statements tend to help the jury while detailed and long opening statements by counsel who are deeply familiar with the facts of the case tend to confuse and bore the jury;
- Referring to evidence barred by orders in limine, or to information the parties are not prepared to submit as admissible evidence, is improper;
- Closing arguments must not refer to facts that are not in the record, misstate the evidence, or allude to personal knowledge or opinion;
- No statement should be made to the jury regarding objections made, sustained or overruled; and
- No statement should be made to the jury about opposing counsel's state of mind or motivation.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 14 (docket no. 257) to exclude reference to and evidence of a 1985 material safety data sheet (MSDS) addressing exposure to medroxyprogesterone acetate (MPA) is DENIED. The MSDS may be evidence that Upjohn was aware that the substance could aggravate breast cancer, a central issue in this case.

*4 IT IS FURTHER ORDERED that Defendants' motion in limine no. 15 (docket no. 259) to preclude any reference to letters sent to Upjohn by the FDA regarding unrelated advertisements is DENIED at this time. Without seeing the letters, and knowing the context in which they may be used, barring the letters is inappropriate.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 16 (docket no. 261) to bar any reference to the upward and downward sales trends for hormone therapy (HT) before and after the Women's Health Initiative (WHI) report in July 2002 is DENIED. HT sales trends and incidence of breast cancer before and after the WHI report have been regarded as related and are thus relevant to the issue of causation.

IT IS FURTHER ORDERED that Defendants' motion in limine no. 17 (docket no. 263) to exclude from evidence at trial two letters—a letter from the FDA to Upjohn dated August 16, 2000, and the response from Upjohn's counsel dated November 7, 2000 is DENIED. While the motion suggests it seeks to "preclude Plaintiffs from referring directly or indirectly to any FDA letters to Upjohn regarding unrelated hormone therapy drugs," no other letters were discussed in the briefing papers.

All Citations

Not Reported in F.Supp.2d, 2012 WL 12337860

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Exhibit Q

2009 WL 36890
Only the Westlaw citation is currently available.
United States District Court,
N.D. New York.

Harold E. CAMPBELL, JR., Plaintiff,
v.
CONSOLIDATED RAIL CORP.; and
CSX Transportation, Inc., Defendants.

No. 1:05-CV-1501 (GTS/GJD).
|
Jan. 6, 2009.

West KeySummary

1 **Evidence**
Medical testimony

Expert witness's proffered testimony on ergonomics was not completely based on sufficient facts and data. He had reviewed sufficient information to support conclusions and opinions that performing certain jobs generally exposed workers to ergonomic risk factors which had generally been associated with cumulative trauma disorders to the upper extremity. However he had also attempted to draw conclusions and form opinions based on the exposure the specific railroad employee experienced to various ergonomic risk factors without expressly basing those conclusions and opinions on scientific tests or objective measurements. Fed.Rules Evid.Rule 702, 28 U.S.C.A.; Federal Employers' Liability Act, § 1, 45 U.S.C.A. § 51.

1 Cases that cite this headnote

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DECISION and ORDER

GLENN T. SUDDABY, District Judge.

***1** Plaintiff commenced this action on December 28, 2004, pursuant to the Federal Employer's Liability Act ("FELA"), 45 U.S.C. § 51, *et seq.* (*See* Dkt. No. 1, ¶ 4 [Plf.'s Compl.].) Generally, Plaintiff alleges that, while working as a welder during his employment with Defendant railroad companies from September 1976 to June 2005, he was exposed to "excessive and harmful cumulative trauma to his hands." (*See* Dkt. No. 24, ¶ 8 [Plf.'s Am. Compl.].) Plaintiff also alleges that these "injuries were caused in whole or in part by the negligence, carelessness and recklessness of the Defendants and their agents, servants, workmen and/or employees, acting within the scope of their employment." (*Id.* at ¶ 12.)

On or about May 15, 2007, Plaintiff's proffered ergonomics expert, Dr. Robert O. Andres, prepared an expert report offering fourteen (14) "conclusions" and/or "opinions," which are listed below in Part III of this Decision and Order. (Dkt. No. 76, Part 2.) Currently before the Court is Defendants' motion *in limine,* filed on December 15, 2008, seeking to preclude the testimony of Dr. Andres, with regard to each of the referenced fourteen (14) "conclusions" and/or "opinions." (Dkt. No. 76.) On December 22, 2008, Plaintiff filed an opposition to Defendants' motion. (Dkt. No. 86.) On December 29, 2008, Defendants filed a reply. (Dkt. No. 95 .) On December 31, 2008, Plaintiff filed two sur-replies. (Dkt.Nos.103, 105.) On January 5, 2009, the Court conducted a hearing in order to determine (1) whether Dr. Andres is qualified to render his proffered conclusions / opinions, (2) whether the substance of the testimony is reliable, and (3) whether the substance of the testimony

is relevant. For the reasons set forth below, Defendants' motion *in limine* is granted in part and denied in part.

I. GENERAL LEGAL STANDARD

Generally, in order to permit a challenged expert to testify, the Court must conclude that (1) the expert is qualified to render his proffered opinions, (2) the substance of the proffered testimony is reliable, and (3) the substance of the proffered testimony is relevant and not unfairly prejudicial. *See* Fed.R.Evid. 104(a), 401, 403, 702, 703; *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 597, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993); *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 141, 119 S.Ct. 1167, 143 L.Ed.2d 238 (1999).

The proponent of the expert testimony has the burden of establishing that the pertinent admissibility requirements are met by a preponderance of the evidence. *See* Fed.R.Evid. 702, Advisory Committee Notes: 2000 Amendments; *Topliff v. Wal-Mart Stores East LP*, 04-CV-0297, 2007 WL 911891, at *3 & n. 5 (N.D.N.Y. Mar.22, 2007) (Lowe, M.J.) [citations omitted]. It is true that, generally, such a proponent is aided by the presumption of admissibility of evidence. *Topliff*, 2007 WL 911891, at *3 & n. 6 [citations omitted]. However, even this presumption will not rescue a proponent who has failed to adduce sufficient evidence in support of his position. *Id.* at *3 & n. 7 [collecting cases]. Finally, it should be noted that "the standards for determining the reliability and credibility of expert testimony are not altered [in FELA cases] merely because the burden of proof is relaxed." *Higgins v. Consol. Rail Corp.*, 06-CV-0689, 2008 WL 5054224, at *2 (N.D.N.Y. Nov.21, 2008) (Sharpe, J.) [citation omitted].

II. ANALYSIS

A. Whether Dr. Andres Is Qualified to Render His Proffered Opinions

***2** "To determine whether a witness qualifies as an expert, courts compare the area in which the witness has superior knowledge, education, experience, or skill with the subject matter of the proffered testimony." *U.S. v. Tin Yat Chin*, 371 F.3d 31, 40 (2d Cir.2004) [citation omitted]. "In assessing whether a proposed expert is 'qualified,' the trial judge should remember the 'liberal [ ] purpose' of Rule 702, and remain 'flexibl[e]' in evaluating the proposed expert's qualifications." *Topliff*, 2007 WL 911891, at *3 & n. 8 [citations omitted]. "As long as some reasonable indication of qualification is adduced, the court may admit the evidence without abdicating its gate-keeping function." *Rushing v. Kansas City S. Ry. Co.*, 185 F.3d 496, 507 (5th Cir.1999).

Here, Plaintiff has provided Dr. Andres' educational background and professional experience in some detail. (Dkt. No. 76, Part 3.) In addition, Defendants appear to concede that Dr. Andres is qualified as an expert in ergonomics, focusing only on the reliability and relevance of his proffered testimony. (Dkt. No. 76, Part 4, at 2, 6.) The Court notes that it appears that every other federal district court that has addressed the issue has found Dr. Andres to be so qualified. *See Lindquist v. Union Pacific R. Co.*, 07-CV-0027, Memorandum Opinion, at 4 (E.D. Tex. filed Oct. 8, 2008); *Wilcox v. CSX Transp., Inc.*, 05-CV-0107, 2007 WL 1576708, at *15 (N.D.Ind. May 30, 2007); *Williams v. CSX Transp., Inc.*, 03-CV-0348, 2005 U.S. Dist. LEXIS 46024, at *8-16 (N.D.Ind. Aug. 23, 2005); *Thomas v. Reading, Blue Mountain and N. R.R. Co.*, 01-CV-5834, 2003 WL 21949156, at *5-6 (E.D.Pa. Aug.14, 2003); *Tapia v. S. Pac. Transp., Inc.*, 97-CV-1463, Memorandum Opinion and Order, at 8-10 (D.N.M. Sept. 3, 1999); *Aparicio v. Norfolk & Western Ry. Co.*, 93-CV-7261, 1997 U.S. Dist. LEXIS 22886, at *5-6 (N.D.Oh. Aug. 4, 1997); *cf. Pretter v. Metro N. Commuter R.R. Co.*, 206 F.Supp.2d 601, 602-05 (S.D.N.Y.2002) (focusing exclusively on the reliability and relevance of Dr. Andres' proffered testimony, and noting that Dr. Andres does possess at least some "areas of ... expertise").

For these reasons, the Court finds that Dr. Andres is qualified as an expert in ergonomics.

B. Whether Dr. Andres' Testimony Is Reliable

The reliability requirement mentioned above in Part I of this Decision and Order derives from Fed.R.Evid. 702, which provides, in pertinent part, as follows:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert ... may testify ... in the form of opinion or otherwise, if *(1) the testimony is based upon sufficient facts or data, (2) the testimony is*

> *the product of reliable principles and methods, and (3) the witness has applied the principles and methods to the facts of the case.*

Fed.R.Evid. 702 [emphasis added]. As a result, an analysis of whether proffered testimony meets the reliability requirement is generally viewed as involving three inquiries: (1) whether the testimony is based on sufficient facts or data; (2) whether the testimony is the product of reliable principles and methods; and (3) whether the witness has applied the principles and methods reliably to the facts of the case.

1. Whether the Testimony is Based on Sufficient Facts and Data

***3** The first inquiry made in assessing the reliability requirement has to do with sufficiency, specifically, whether the expert's testimony is grounded on sufficient facts and data. This consideration is quantitative rather than qualitative in nature. *See* Fed.R.Evid. 702, Advisory Committee Notes: 2000 Amendments. The term "facts and data" is intended to be broad enough to include (1) the reliable opinions of other experts, and (2) hypothetical facts supported by the evidence. *Id.*

Here, the Court finds that some of Dr. Andres' conclusions and opinions are based on sufficient facts and data. For example, Dr. Andres states that, in preparing his report, he reviewed the following materials: (1) pleadings and deposition testimony in this action (and other actions); (2) medical records of Plaintiff's treating physician; (3) publications on safety, ergonomics or other subjects by the Federal Railroad Administration ("FRA") and the American Association of Railroads ("AAR"); (4) Defendant CSX's description of Plaintiff's job as a welder, and videos of other welders working; (5) Defendant Conrail's other videos and documents; and (6) articles on work-related musculoskeletal disorders, and textbooks on ergonomic risk factors. (*See, e.g.*, Dkt. No. 76, Part 2, at 3-6 [attaching pages "2" to "5" of Dr. Andres' Report].)

As a result, there are sufficient facts and data supporting his conclusions and opinions that performing certain jobs (e.g., welding, etc.) generally exposes workers (and generally exposed Plaintiff) to certain ergonomic risk factors, which generally have been associated with certain cumulative trauma disorders to the upper extremity. (*See generally* Dkt. No. 76, Part 2.) *See also Lovato v. Burlington N. and Sante Fe R.R. Co.*, 00-CV-2584, 2002 WL 1424599, at *7 (D.Colo. June 24, 2002) (permitting expert to testify that the plaintiff, in the course of his normal daily activities as a carman, was routinely and regularly exposed to ergonomic risk factors, which generally have been associated with the development of significant injuries to the forearms, elbows, neck and shoulders).

However, several of Dr. Andres' conclusions and opinions are not based on sufficient facts and data. For example, Dr. Andres attempts to draw certain conclusions, or form certain opinions, based on the "exposure" that Plaintiff experienced to various ergonomic risk factors without expressly basing those conclusions and opinions on scientific tests or objective measurements, such as measurements of (1) the durations and frequency of each of the types of exposures in question, (2) the frequency of specific movements made by Plaintiff, (3) the levels of force used during those movements, (4) the extent of vibration experienced by Plaintiff during specific tasks, (5) the rest periods in between tasks, (6) the extent of stress to Plaintiff's hands, and/or (7) the air temperature. (*Id.*) The omission of such measurements is conspicuous since Dr. Andres testified, at the *Daubert* hearing, that it was generally possible to measure such things as (1) the different angles involved in various postures, (2) the levels of vibration from using various tools (e.g., "grinders," etc.), and (3) the amount of repetition involved in various jobs. Rather, Dr. Andres generally bases these conclusions and opinions on the following: (1) a comparison of Plaintiff's description of his own work to a visual inspection of work performed by other persons at other work sites (which are mostly operated by other railroad companies); (2) a weighing of tools similar to those presumably used by Plaintiff; and (3) a checking of boxes on an ergonomic checklist for the presence of "force exerted," "awkward postures," and "vibration." (*Id; see also Daubert* Hearing Testimony.) Several federal courts have been critical of drawing certain conclusions, or forming certain opinions, on such "facts and data." *See, infra,* note 1 of this Decision and Order (citing cases).

***4** For these reasons, the Court finds that, while some of Dr. Andres' conclusion and opinions are based on sufficient facts and data, others-which are described in more detail below in Part III of this Decision and Order-are not based on sufficient facts and data.

2. Whether Dr. Andres' Testimony Is the Product of Reliable Principles and Methods, and Whether He Has Applied the Principles and Methods Reliably to the Facts of the Case

The second and third inquiries made in assessing the reliability requirement are qualitative in nature, requiring that the principles and methods be both reliable in and of themselves and reliably applied to the facts of the case. Courts have considered various factors as indicators of whether these two requirements have been satisfied. The Supreme Court has stated that, in considering the applicable factors, a court's ultimate objective is "to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Kumho Tire,* 526 U.S. at 151.

Generally, these factors include the following: (1) whether the expert's technique or theory can be, or has been, tested-that is, whether the expert's theory can be challenged in some objective sense, or whether it is instead simply a subjective, conclusory approach that cannot reasonably be assessed for reliability; (2) whether the technique or theory has been subject to peer review and publication; (3) the known or potential rate of error of the technique or theory when applied; (4) the existence and maintenance of standards and controls; (5) whether the technique or theory has been generally accepted in the scientific community; (6) whether the expert is proposing to testify about matters growing naturally and directly out of research they have conducted independent of the litigation, or whether they have developed their opinions expressly for the purposes of testifying; (7) whether the expert has unjustly extrapolated from an accepted premise to an unfounded conclusion; and (8) whether the expect has adequately accounted for obvious alternative explanations for the plaintiff's condition. *See Daubert v. Merrell Dow Pharm., Inc.,* 509 U.S. 579, 593-94, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993) [citations omitted]; *Topliff,* 2007 WL 911891, at *13-14 & nn. 89-93 [citations omitted]; Fed.R.Evid. 702, Advisory Committee Notes: 2000 Amendments.

Here, the Court finds that some of Dr. Andres' testimony is the product of a reliable application of reliable principles and methods, e.g., his testimony that performing the jobs that Plaintiff performed generally exposes workers (and generally exposed Plaintiff) to certain ergonomic risk factors, which generally have been associated with certain cumulative trauma disorders to the upper extremity. (*See generally* Dkt. No. 76, Part 2.) *See Lovato,* 2002 WL 1424599, at *7 (D.Colo. June 24, 2002) (permitting expert to testify that the plaintiff, in the course of his normal daily activities as a carman, was routinely and regularly exposed to ergonomic risk factors, which generally have been associated with the development of significant injuries to the forearms, elbows, neck and shoulders).

***5** However, some of Dr. Andres' testimony is not the product of a reliable application of reliable principles and methods. For example, any conclusion or opinion offered by Dr. Andres (whether explicitly or implicitly) that Plaintiff's jobs, work conditions or training *caused* his cumulative trauma disorder is unreliable for a number of reasons, including the following: (1) the fact that such a theory is not the result of testing by Dr. Andres but rather is simply a subjective, conclusory approach that cannot reasonably be assessed for reliability; (2) the fact that there is no known or potential rate of error of the analytical technique used by Dr. Andres; and (3) the fact that Dr. Andres has not adequately accounted for obvious alternative explanations for Plaintiff's condition (such as medical histories and non-work activities). *See Magdaleno v. Burlington N. R.R. Co.,* 5 F.Supp.2d 899, 902-04 (D.Colo.1998) (precluding expert from testifying that the plaintiff's working conditions caused the cumulative trauma disorder to his wrists and hands, because, *inter alia,* he failed to consider non-occupational factors, such as medical histories and non-work activities, as the cause of the plaintiff's injuries); *Lovato,* 2002 WL 1424599, at *7-8 (precluding expert from testifying that risk factors present in plaintiff's work were sufficient to cause, or did cause, plaintiff's injuries, because of, *inter alia,* lack of testing).

For these reasons, the Court finds that, while some of Dr. Andres' conclusions and opinions are the product of a reliable application of reliable principles and methods, others-which are described in more detail below in Part III of this Decision and Order-are not the product of a reliable application of reliable principles and methods.

C. Whether Dr. Andres' Testimony Is Relevant and Not Unfairly Prejudicial

The Federal Rules of Evidence provide that " '[r]elevant evidence' means evidence having any tendency to make the existence of any fact that is of consequence to

the determination of the action more probable or less probable than it would be without the evidence." Fed.R.Evid. 401. The Federal Rules of Evidence further provide that "[a]ll relevant evidence is admissible, except as otherwise provided by ... these rules." Fed.R.Evid. 402. One of the rules that excludes relevant evidence under certain circumstances is Fed.R.Evid. 403, which provides as follows: "Although relevant, evidence may be excluded if its probative value is substantially outweighed by the danger of unfair prejudice, confusion of the issues or misleading the jury, or by considerations of undue delay, waste of time, or needless presentation of cumulative evidence." Fed.R.Evid. 403. Given that "[e]xpert evidence can be both powerful and quite misleading because of the difficulty in evaluating it ..., the judge in weighing possible prejudice against probative force under Rule 403 ... exercises more control over experts than over lay witnesses." *Daubert,* 509 U.S. 595 [internal quotation marks and citation omitted].

***6** Here, some of Dr. Andres' testimony (i.e., the testimony described with approval in Parts II.B.1. and II.B.2. of this Decision and Order) would be relevant and not unfairly prejudicial. However, some of his testimony would be unfairly prejudicial. For example, any probative value from Dr. Andres' testimony that Defendants "should have" conducted or implemented certain evaluations, training or programs would be substantially outweighed by the danger of unfair prejudice, confusion of the issues or misleading the jury. *See Pretter v. Metro North Commuter R.R. Co.,* 206 F.Supp.2d 601, 603-04 (S.D.N.Y.2002) (precluding Dr. Andres from using words "should have" since it was not a matter reducible to scientific certainty and was calculated to confuse and mislead the jury).

For these reasons, the Court finds that, while some of Dr. Andres' conclusions and opinions are relevant and not unfairly prejudicial, others-which are described in more detail below in Part III of this Decision and Order-are unfairly prejudicial.

III. SPECIFIC RULINGS

Conclusion / Opinion 1: "Mr. Campbell has a medical history consistent with exposure to ergonomic risk factors for the upper extremity."

This conclusion / opinion is precluded in part for four reasons: (1) the term "medical history" is vague and refers to a subject outside Dr. Andres' area of expertise; (2) the term "consistent with" implies a causal relationship without a scientific basis; (3) the asserted "exposure" was not objectively measured by Dr. Andres with regard to the duration of each such type of exposure, the frequency of such exposures, the frequency of movements, the levels of force used, the rest periods in between, but was derived from a visual inspection of work performed by other persons at another work site; and (4) the term "ergonomic risk factors" is not defined with specificity. [1]

1 *See Pretter v. Metro North Commuter R.R. Co.,* 206 F.Supp.2d 601, 603-04 (S.D.N.Y.2002) (precluding Dr. Andres from testifying that plaintiffs had a work history consistent with exposure to ergonomic risk factors, because conclusion was vague and term "ergonomic risk factors" [1] was not defined with specificity, and [2] was not measured with objectivity as to frequency of movements or levels of force used, but rather was derived from visual inspection of work functions); *Lovato v. Burlington N. and Sante Fe R.R. Co.,* 00-CV-2584, 2002 WL 1424599, at *6-9 (D.Colo. June 24, 2002) (precluding expert from testifying that risk factors present in plaintiff's work were sufficient to cause, or did cause, plaintiff's injuries, because expert did not measure vibration or forces generated by tools that plaintiff used, did not know how much time plaintiff used the tools, and visited plaintiff's work site only once before reaching his conclusion); *Stasior v. Nat'l R.R. Passenger Corp.,* 19 F.Supp.2d 835, 849-51 (N.D.Ill.1998) (precluding expert from testifying that the plaintiff's awkward posture and repetition at the railroad's workstation contributed to the plaintiff's carpal tunnel syndrome and chronic tendonitis, because expert did not test or quantify the degree of awkward posture and repetition which the plaintiff allegedly suffered); *Magdaleno v. Burlington N. R.R. Co.,* 5 F.Supp.2d 899, 902-04 (D.Colo.1998) (precluding expert from testifying that the plaintiff's working conditions caused the cumulative trauma disorder to his wrists and hands, because he failed to [1] measure the plaintiff's body, [2] measure the duration, joint deviation, posture, or force exertion necessary to operate the specific tools used by the plaintiff, [3] measure temperature of the repair facility at which the plaintiff worked, [4] measure the recovery time permitted for company employees after their use of a specific tool, and [5] failed to consider non-occupational factors, such as medical histories and non-work activities, as the cause of the plaintiff's injuries).

As a possible alternative, Dr. Andres may offer testimony consistent with the following (if appropriate): "Performing the job of welding generally exposes workers to certain ergonomic risk factors (i.e., [list factors]), which generally have been associated with (among other injuries and/or illnesses) cumulative trauma disorder to the upper extremity."

Conclusion / Opinion 2: "Mr. Campbell has been exposed to repetitive work using vibrating hand tools in several of his job tasks. This repetitive work was hand intensive, required forceful exertions, and required prolonged awkward postures of and mechanical stress concentrations to the upper extremity. Welding tasks also required sustained awkward postures of the knees, as well as lifting and carrying. Gloves were worn for most tasks, and some of his work was done in cold conditions."

This conclusion / opinion is generally permissible but is precluded in part for two reasons: (1) the asserted "exposure" was not objectively measured by Dr. Andres with regard to the duration of each such type of exposure, the frequency of such exposures, the frequency of movements, the levels of force used, the rest periods in between, the extent of vibration, the extent of stress to the hands, and the air temperature, but was derived from a visual inspection of work performed by other persons at another work site; and (2) the terms "knees," "lifting" and "carrying" are no longer relevant because the plaintiff has withdrawn his claim regarding his lower extremity. [2]

2 *See Pretter,* 206 F.Supp.2d at 603-04 (precluding Dr. Andres from testifying that the jobs performed by the plaintiffs exposed them to sufficient amount of documented ergonomic risk factors for the upper extremity to be consistent with the development of Carpal Tunnel Syndrome, because conclusion was vague, and the ergonomic risk factors were not measured with objectivity as to frequency of movements or levels of force used, but rather derived from visual inspection of work functions); *Baker v. Metro-North R.R. Co.,* 98-CV-1073, 2003 WL 22439730, at *2 (D.Conn. Oct.23, 2003) (precluding expert from testifying because she failed to measure ergonomic risk factors, and did not ascertain rest period between the plaintiff's exposure to the risks); *Stasior,* 19 F.Supp.2d at 849-51 (precluding expert from testifying that the plaintiff's awkward posture and repetition at the railroad's workstation contributed to the plaintiff's carpal tunnel syndrome and chronic tendonitis, because expert did not test or quantify the degree of awkward posture and repetition which the plaintiff allegedly suffered); *cf. Lovato,* 2002 WL 1424599, at *6-7 (allowing expert to conclude that, in the course of the plaintiff's normal daily activities at work, he was routinely and regularly exposed to ergonomic risk factors because this conclusion stemmed from the expert's observations of the plaintiff at work).

*7 As an alternative, Dr. Andres may offer testimony consistent with the following (if appropriate): "Based on what I have learned and observed, including my knowledge of Mr. Campbell's work, it appears to me that, during the relevant time period, generally Mr. Campbell was exposed to repetitive work using vibrating hand tools in several of his job tasks. This repetitive work was hand intensive, required forceful exertions, and required prolonged awkward postures of and mechanical stress concentrations to the upper extremity. Gloves were worn for most tasks, and some of his work was done in cold conditions."

Conclusion / Opinion 3: "Based on materials I have seen, Conrail/CSX did not perform an ergonomic screening or job analysis of many of the jobs that Mr. Campbell performed prior to his injuries or occupational illnesses."

This conclusion / opinion is precluded in part for four reasons: (1) Dr. Andres has no personal knowledge of what screening or analysis Defendants did or did not do; (2) the term "many of the jobs" is subjective and vague; (3) the term "prior to his injuries" is vague as to time, and implies causal relationship without scientific justification; and (4) Dr. Andres' assertion that the ergonomic screening or job analysis never occurred implies that it should have occurred (in fulfillment of a legal duty under FELA), which is a notion not reducible to scientific certainty, and which is calculated to confuse and mislead the jury. [3]

3 *See Pretter,* 206 F.Supp.2d at 603-04 (precluding Dr. Andres from testifying that none of the plaintiffs had ever received ergonomics training beyond safety meetings on the job, because of lack of personal knowledge); *Magdaleno,* 5 F.Supp.2d at 906 (precluding expert from testifying that defendants should conduct a detailed analysis of the workplace then institute changes, because testimony improperly opines on causation).

As possible alternatives, Dr. Andres may offer testimony consistent with the following (if appropriate): (1) "Generally, to mitigate the effects of certain ergonomic risk factors for cumulative trauma disorders to the upper extremity, it is recommended by [state whom (e.g., Occupational Safety and Health Administration ("OSHA"), the FRA, the AAR, and/or me in my expert opinion)] that a company perform the following ergonomic screening or job analysis: [describe]"; and (2) "Based on the materials I have seen, it appears to me that, during the relevant time period, Defendants generally did not perform such an ergonomic screening or job analysis for certain jobs in the following regard: [describe]."

Conclusion / Opinion 4: "Mr. Campbell never received ergonomic training concerning the upper or lower extremity beyond safety meetings or on the job. He was not trained to recognize upper or lower extremity ergonomic risk factors in his job or how to minimize their effect. He was not trained to recognize early musculoskeletal disorders, nor was any step taken by management when he reported these symptoms at their onset."

This conclusion / opinion is precluded in part for four reasons: (1) Dr. Andres has no personal knowledge of what training Mr. Campbell did or did not receive; (2) the term "when he reported these symptoms at their onset" is vague as to time; (3) Dr. Andres has no personal knowledge of what steps Defendants did or did not take in response to any reported symptoms by Plaintiff; and (4) Dr. Andres' assertion that the ergonomic training in question never occurred implies that it should have occurred (in fulfillment of a legal duty under FELA), which is a notion not reducible to scientific certainty, and which is calculated to confuse and mislead the jury. [4]

4 *See Pretter,* 206 F.Supp.2d at 603-04 (precluding Dr. Andres from testifying that none of the plaintiffs had ever received ergonomics training beyond safety meetings on the job, because of lack of personal knowledge; and precluding Dr. Andres from using words "should have" since it was not a matter reducible to scientific certainty and was calculated to confuse and mislead the jury).

***8** As possible alternatives, Dr. Andres may offer testimony consistent with the following (if appropriate): (1) "Generally, to mitigate the effects of certain ergonomic risk factors for the upper extremity, it is recommended [state whom (e.g., OSHA, the FRA, the AAR, and/or me in my expert opinion)] that a company administer the following ergonomic training to its employees: [describe]"; and (2) "Based on the materials I have seen, it appears to me that, during the relevant time period, Defendants generally did not administer such ergonomic training in the following regard: [describe]."

Conclusion / Opinion 5: "Conrail/CSXT has not implemented any comprehensive plan to control the hazards of exposure to lower and upper extremity ergonomic risk factors for welders like Mr. Campbell."

This conclusion / opinion is precluded for four reasons: (1) Dr. Andres has no personal knowledge of what plan Defendant did or did not have; (2) Dr. Andres' assertion that Defendants did not implement the plan in question implies that they should have implemented such a plan (in fulfillment of a legal duty under FELA), which is a notion not reducible to scientific certainty, and which is calculated to confuse and mislead the jury; (3) the term "comprehensive" is vague and subjective; and (4) the term "lower extremity" is no longer relevant because Plaintiff has withdrawn his claim regarding his lower extremity. [5]

5 *See Pretter* 206 F.Supp.2d at 603-04 (precluding Dr. Andres from testifying that the railroad failed to perform a job analysis of the jobs employees performed and that various departments did not effectively communicate with each other because of lack of personal knowledge); *Thomas v. Reading, Blue Mountain and N. R.R. Co.,* 01-CV-5834, 2003 WL 21949156, at *5 (E.D.Pa. Aug.14, 2003) (precluding any conclusion or opinion that Conrail lacked a proper program and/or evaluation-process [e.g., "screening program," "training program," "hazard-control program," "ergonomics program," "worksite and job evaluations," etc.] unless Dr. Andres was able to indicate precisely what proper program and/or evaluation process would have been, and that he is certain that Conrail in fact did not have such program and/or evaluation process).

As possible alternatives, Dr. Andres may offer testimony consistent with the following (if appropriate): (1) "Generally, to mitigate the effects of certain ergonomic risk factors for cumulative trauma disorders to the upper extremity, it is recommended by [state whom (e.g., OSHA, the FRA, the AAR, and/or me in my expert opinion)] that a company implement the following plan to control the hazards of exposure to those ergonomic risk factors for

welders: [describe]"; and (2) "Based on the materials I have seen, it appears to me that, during the relevant time period, Defendants generally did not implement such a plan in the following regard: [describe]."

Conclusion / Opinion 6: "Conrail/CSXT does not have a comprehensive ergonomics program consistent with published guidelines for the prevention of WMSDs [work-related musculoskeletal disorders]."

This conclusion / opinion is precluded in part for six reasons: (1) Dr. Andres has no personal knowledge of what program Defendant did or did not have; (2) his use of the present tense renders his conclusion / opinion irrelevant in that the period of time at issue is before June 27, 2005, when Plaintiff ceased his employment with Defendants; (3) Dr. Andres' assertion that Defendants did not have the program in question implies that they should have had such a program (in fulfillment of a legal duty under FELA), which is a notion not reducible to scientific certainty, and which is calculated to confuse and mislead the jury; (4) the term "comprehensive" is vague and subjective; (5) the term "published guidelines" is vague; and (6) the term "work-related musculoskeletal disorders" is too vague or broad since the only injuries or illnesses that are relevant under the circumstances are those for a cumulative trauma disorders to the upper extremity. [6]

6 *See Pretter,* 206 F.Supp.2d at 603-04 (precluding Dr. Andres from using words "should have" since it was not a matter reducible to scientific certainty and was calculated to confuse and mislead the jury; and precluding Dr. Andres from testifying that the railroad did not provide certain training, or have a certain program, because of lack of personal knowledge); *Thomas,* 2003 WL 21949156, at *5 (precluding any conclusion or opinion that Conrail lacked a proper program and/or evaluation-process [e.g., "screening program," "training program," "hazard-control program," "ergonomics program," "worksite and job evaluations," etc.] unless Dr. Andres was able to indicate precisely what proper program and/or evaluation process would have been, and that he is certain that Conrail in fact did not have such program and/or evaluation process).

***9** As possible alternatives, Dr. Andres may offer testimony consistent with the following (if appropriate): (1) "Generally, to prevent certain work-related musculoskeletal disorders to the upper extremity, it is recommended by [state whom (e.g., OSHA, the FRA, the AAR, and/or me in my expert opinion)] that a company have an ergonomics program consistent with the following ergonomics-program guidelines that have been published (i.e., [describe guidelines and specify by whom published])"; and (2) "Based on the materials I have seen, it appears to me that, during the relevant time period, Defendants generally did not have such a program in the following regard: [describe]."

Conclusion / Opinion 7: "Mr. Campbell was exposed to documented ergonomic risk factors for the upper extremity. These risk factors included forceful gripping, segmental vibration, and awkward postures. This type of exposure has been associated with the development of CTS and osteoarthritis."

This conclusion / opinion is precluded in part for the following reason: the asserted "exposure" and "ergonomic risk factors" were not objectively measured by Dr. Andres with regard to the duration of each such type of exposure, the frequency of such exposures, the frequency of movements, the levels of force used, the rest periods in between, the extent of vibration, or the extent of stress to the hands, but was derived from a visual inspection of work performed by other persons at another work site. [7]

7 *See, supra,* note 2 (citing *Lovato* case); *Magdaleno,* 5 F.Supp.2d at 906 (permitting expert to testify that four risk factors contribute to cumulative trauma disorders because ample support exists in the scientific community to reach this conclusion).

As a possible alternative, Dr. Andres may offer testimony consistent with the following (if appropriate): "Based on what I have learned and observed, including my knowledge of Mr. Campbell's work, it appears to me that, during the relevant time period, generally Mr. Campbell was exposed to documented ergonomic risk factors for the upper extremity. These risk factors included forceful gripping, segmental vibration, and awkward postures. Generally, this type of exposure has been associated with the development of Carpal Tunnel Syndrome and osteoarthritis."

Conclusion / Opinion 8: "Mr. Campbell was exposed to documented ergonomic risk factors for the lower extremity. These risk factors included lifting, carrying, squatting, kneeling, and walking on uneven surfaces."

This conclusion / opinion is precluded on grounds relevance and unfair prejudice because it deals only with lower extremity risk factors. Plaintiff has withdrawn his claim regarding his lower extremity.

Conclusion / Opinion 9: "Exposure to lifting, carrying, squatting, kneeling, and walking on uneven surfaces has been associated with accelerated joint degeneration and the development of knee osteoarthritis."

This conclusion / opinion is precluded on grounds relevance and unfair prejudice because it deals only with lower extremity risk factors. Plaintiff has withdrawn his claim regarding his lower extremity.

Conclusion / Opinion 10: "Walking on main line ballast created greater stresses within the lower extremities of Mr. Campbell than walking on walkway ballast of flat level surfaces."

***10** This conclusion / opinion is precluded on grounds relevance and unfair prejudice because it deals only with lower extremity risk factors. Plaintiff has withdrawn his claim regarding his lower extremity.

Conclusion / Opinion 11: "Conrail/CSXT should have but did not perform comprehensive worksite and job evaluations for ergonomic risk factors to which welders like Mr. Campbell were exposed. If such analyses had been completed, or if Conrail/CSXT had heeded previous research, Conrail/CSXT would have known that some of these job tasks increased the risk of WMSDs for workers such as Mr. Campbell and systematic control strategies should have been implemented."

This conclusion / opinion is precluded in part for six reasons: (1) the term "should have ... perform[ed] ... evaluations" implies that Defendants had a legal duty to Plaintiff under FELA to perform such evaluations, which is not a matter reducible to scientific certainty, and which is calculated to confuse and mislead the jury; (2) Dr. Andres has no personal knowledge of what evaluations Defendant did or did not perform; (3) the referenced "exposure" was not objectively measured by Dr. Andres with regard to the duration of each such type of exposure, the frequency of such exposures, the frequency of movements, the levels of force used, the rest periods in between, but was derived from a visual inspection of work performed by other persons at another work site; (4) the term "comprehensive" is vague and subjective; (5) the term "previous research" is vague; and (6) the assertion is speculative in nature as to whether performing worksite and job evaluations would have impacted Mr. Campbell, and what Defendant "would have known" had it "heeded" previous research. [8]

8 *See, supra,* note 6 (citing *Pretter* case).

As possible alternatives, Dr. Andres may offer testimony consistent with the following (if appropriate): (1) "Generally, the association between certain ergonomic risk factors (i.e., [define]) and cumulative trauma disorders to the upper extremity is known in American industry due to having been widely published in the following trade and scientific journals: [specify]"; (2) "Generally, to mitigate the effects of certain ergonomic risk factors for the upper extremity to which welders are exposed, it is recommended by [state whom (e.g., OSHA, the FRA, the AAR, and/or me in my expert opinion)] that a company perform the following worksite and job evaluations for those ergonomic risk factors: ([describe evaluations])"; and (3) "Based on the materials I have seen, it appears to me that, during the relevant time period, Defendants generally did not perform such evaluations in the following regard: [describe]."

Conclusion / Opinion 12: "Conrail/CSXT should have but did not provide adequate training to Mr. Campbell to empower him to minimize exposure to upper and lower extremity ergonomic risk factors and to recognize early signs and symptoms of upper and lower extremity musculoskeletal disorders."

***11** This conclusion / opinion is precluded in part for four reasons: (1) the term "should have ... provide[d] ... training" implies that Defendants had a legal duty to Plaintiff under FELA to provide such training, which is not a matter reducible to scientific certainty, and which is calculated to confuse and mislead the jury; (2) Dr. Andres has no personal knowledge of what training Defendants did or did not provide Plaintiff; (3) the term "lower extremity" is no longer relevant because Plaintiff has withdrawn his claim regarding his lower extremity; and (4) the terms "adequate training," "minimize," and "early" are vague and subjective. [9]

9 *See, supra,* note 6 (citing cases).

As possible alternatives, Dr. Andres may offer testimony consistent with the following (if appropriate): (1) "Generally, to mitigate the effects of certain ergonomic risk factors to the upper extremity, it is recommended by [state whom (e.g., OSHA, the FRA, the AAR, and/or me in my expert opinion)] that a company provide the following training to its employees to enable them to recognize the signs and symptoms of a cumulative trauma disorder to the upper extremity: [describe training]"; and (2) "Based on the materials I have seen, it appears to me that, during the relevant time period, Defendants generally did not provide such training in the following regard: [describe]."

Conclusion / Opinion 13: "Conrail/CSXT should have but did not implement a medical management program, including early reporting of muscoloskeletal disorders of a non-traumatic origin, conservative return to work, and medical monitoring, to treat and control lower and upper extremity work related muscoloskeletal disorders."

This conclusion / opinion is precluded in part for four reasons: (1) the term "should have ... implement[ed] a medical monitoring program" implies that Defendants had a legal duty to Plaintiff under FELA to implement such a program, which is not a matter reducible to scientific certainty, and which is calculated to confuse and mislead the jury; (2) Dr. Andres has no personal knowledge of what program Defendants did or did not implement; (3) the term "early" is vague and subjective; and (4) the term "lower extremity" is no longer relevant because Plaintiff has withdrawn his claim regarding his lower extremity. [10]

10 *See, supra,* note 6 (citing cases).

As possible alternatives, Dr. Andres may offer testimony consistent with the following (if appropriate): (1) "Generally, to treat and control certain upper-extremity work-related muscoloskeletal disorders of a non-traumatic origin, it is recommended by [state whom (e.g., OSHA, the FRA, the AAR, and/or me in my expert opinion)] that a company implement the following medical management program: [describe]"; and (2) "Based on the materials I have seen, it appears to me that, during the relevant time period, Defendants generally did not implement such a program in the following regard: [describe]."

Conclusion / Opinion 14: "Conrail/CSXT did not have a comprehensive ergonomic program that a reasonable employer should have had in place to protect Mr. Campbell."

***12** This conclusion / opinion is precluded in part for four reasons: (1) Dr. Andres has no personal knowledge of what ergonomics program Defendants did or did not have; (2) the term "comprehensive" is vague and subjective; (3) whether or not Defendants acted as a "reasonable employer" is a finding of fact for the jury; and (4) the term "should have had in place [an ergonomics program]" implies that Defendants had a legal duty to Plaintiff under FELA to have such a program, which is not a matter reducible to scientific certainty, and which is calculated to confuse and mislead the jury. [11]

11 *See, supra,* note 6 (citing *Pretter* case).

As possible alternatives, Dr. Andres may offer testimony consistent with the following (if appropriate): (1) "Generally, to prevent cumulative trauma disorders to the upper extremity, it is recommended by [state whom (e.g., OSHA, the FRA, the AAR, and/or me in my expert opinion)] that a company have the following ergonomics program: [describe]"; and (2) "Based on the materials I have seen, it appears to me that, during the relevant time period, Defendants generally did not have such a program in the following regard: [describe]."

ACCORDINGLY, it is

ORDERED that Defendants' motion *in limine* to preclude the testimony of Plaintiff's ergonomics expert, Dr. Robert O. Andres, with regard to each of the fourteen (14) "conclusions" and/or "opinions" he offers in his expert report (Dkt. No. 76) is ***GRANTED*** in part and ***DENIED*** in part, as described in Part III of this Decision and Order.

All Citations

Not Reported in F.Supp.2d, 2009 WL 36890

End of Document

Exhibit R

2010 WL 654287
Only the Westlaw citation is currently available.
United States District Court,
S.D. Ohio,
Western Division.

Elwood H. JONES, Jr., Petitioner,
v.
Margaret BAGLEY, Warden, Respondent.

No. C–1:01–cv–564.
|
Feb. 19, 2010.

Attorneys and Law Firms

Michael Lloyd Monta, Monta & Monta, Gary Wayne Crim, Dayton, OH, for Petitioner.

Sarah Lyn Leatherman, Stephen E. Maher, Office of the Ohio Attorney General, Criminal Justice Section Capital Crimes Unit, Columbus, OH, for Respondent.

ENTRY AND ORDER OVERRULING JONES'S OBJECTIONS (Doc. # 162) TO THE MAGISTRATE JUDGE'S REPORT AND RECOMMENDATIONS; ADOPTING THE MAGISTRATE JUDGE'S REPORT AND RECOMMENDATIONS (Doc. # 160) IN ITS ENTIRETY; AND DISMISSING JONES'S PETITION FOR A WRIT OF HABEAS CORPUS WITH PREJUDICE

THOMAS M. ROSE, District Judge.

***1** This matter comes before the Court pursuant to Petitioner Elwood H. Jones Jr.'s ("Jones's") Objections to Magistrate Judge Michael R. Merz's Report and Recommendations. The Report and Recommendations was entered on August 31, 2009. (Doc. # 166.) On November 16, 2009, Jones filed objections. (Doc. 162.) On February 2, 2010, the Warden responded to Jones's Objections. (Doc. # 165.) Jones's Objections are, therefore, ripe for decision.

As required by 28 U.S.C. § 636(b) and Federal Rules of Civil Procedure Rule 72(b), the District Judge has made a de novo review of the record in this case. Upon said review, the Court finds that Jones's Objections to the Magistrate Judge's Report and Recommendations are not well-taken, and they are hereby OVERRULED. The Magistrate Judge's Report and Recommendations is adopted in its entirety. Finally, Jones's Petition for a Writ of Habeas Corpus is DENIED with prejudice.

DONE and **ORDERED.**

REPORT AND RECOMMENDATIONS ON THE MERITS

MICHAEL R. MERZ, United States Magistrate Judge.

This capital habeas corpus case is before the Magistrate Judge for report and recommendations on the merits.

Procedural History in the Ohio Courts

Petitioner was indicted on September 27, 1995, by the Hamilton County Grand Jury on four counts, including two counts of aggravated murder for violations of the Ohio Revised Code § 2903.01(B) (murder while committing aggravated robbery and aggravated burglary). Each aggravated murder count had two death penalty specifications, that the victim was killed during the commission of aggravated burglary and aggravated robbery and that the defendant acted as the principal offender or with prior calculation and design. The third count charged aggravated burglary with a specification for inflicting physical harm in violation of Ohio Revised Code § 2929.11(A)(1) and the fourth count charged aggravated robbery in violation of Ohio Revised Code § 2911.01(A)(2). Both of these counts contained prior burglary conviction specifications.

Trial commenced on November 12, 1996, and the jury found Jones guilty on November 26, 1996. After a sentencing hearing the jury recommended imposition of the death penalty. The court accepted the jury's recommendation on January 9, 1997, and sentenced Jones to death for the two counts of aggravated murder and fifteen to twenty-five years for the aggravated burglary and aggravated robbery charges.

The Ohio Supreme Court summarized the facts as follows:

During the early afternoon of Friday, September 2, 1994, Elaine Schub and Joe Kaplan checked in as guests at the Embassy Suites Hotel in Blue Ash. Schub was in town to see her grandson's bar mitzvah, which was to be held the following day. Schub's best friend, Rhoda Nathan, flew in from New Jersey later that afternoon also to attend the event on Saturday. Schub and Nathan shared the bedroom of the hotel suite, while Kaplan stayed in the front room using a foldout bed.

***2** On Saturday morning, September 3, Schub and Kaplan awoke early to meet relatives at the complimentary breakfast served on the first floor of the hotel. As she and Kaplan left the room at approximately 7:28 a.m., Schub told Nathan to go back to sleep, since she did not need to be at the temple that morning as early as the family. Kaplan had the only room key for the group and made sure the door was locked when he and Schub left for breakfast.

At approximately 8:08 a.m., Schub and Kaplan finished breakfast and returned upstairs to their room. Kaplan unlocked the door and discovered Nathan lying nude on the floor. Employees and hotel guests rushed up to Room 237, where Schub was found screaming and shaking. A cardiologist, a respiratory therapist, and a nurse happened to be at the hotel at the time, and they came to the room to help resuscitate Nathan.

Initially, witnesses thought Nathan had had a fall, perhaps brought on by a heart attack, since there seemed to be little blood on or around Nathan. However, further investigation revealed that Nathan's hair was soaked with blood and that she had suffered severe trauma to her head. When Nathan's head was moved, witnesses found a tooth on the floor. Later, Schub asked for and was given her purse, which she had left in the hotel room during breakfast. Upon opening her wallet, which was inside the purse, Schub noticed that money was missing. During the commotion, Schub noticed that Nathan no longer had the pendant necklace that she had been wearing earlier and that she always wore. The pendant was a one-of-a-kind piece of jewelry that Nathan's late husband had made from his mother's wedding band. It consisted of several connected gold bars, one containing the diamonds. According to Nathan's daughter-in-law, Nathan never took the pendant off. Nathan died that afternoon as a result of multiple traumas to her head and body. The coroner's office determined that the death was a homicide.

Police quickly set up a command center in a banquet room on the second floor near the murder scene in Room 237. Police canvassed the rooms at the hotel and took statements from guests and hotel employees working that day. Police then began to concentrate their investigation on three particular hotel employees who had prior criminal histories. Police cleared two of the employees through further investigation and narrowed their investigation to defendant-appellant, Elwood "Butch" Jones. Police discovered from interviews with other hotel employees that appellant had injured his hand on the day Nathan was killed. This fact pointed to appellant as a suspect because the crime at the hotel involved a violent assault. Appellant had filed a claim for workers' compensation for medical benefits. The police thereafter subpoenaed and received the medical records for the treatment of appellant's hand injury.

On September 12, 1994, Sgt. Robert Lilley of the Blue Ash Police Department spoke with one of appellant's treating physicians, Dr. John McDonough. Lilley learned through another police investigator that Dr. McDonough had classified appellant's injury as a fist-tomouth injury and that Dr. McDonough had asked appellant if he received the injury by punching someone in the mouth. That same day, police went to the residence of Earlene Metcalfe in Loveland. Metcalfe worked at the hotel and was a girlfriend of appellant, in addition to being listed as a witness to appellant's hand injury on his workers' compensation claim form. Upon arriving at Metcalfe's residence, police found appellant there, and both he and Metcalfe voluntarily agreed to answer questions at the Blue Ash Police station concerning the homicide at the hotel.

***3** At the police station, appellant was advised of his *Miranda* rights and signed a waiver form. During the interview with Sgt. Lilley and Blue Ash Police Officer Larry Stokes, appellant stated that he and Metcalfe arrived at the hotel on September 3 at approximately 5:00 a.m. At that time, appellant signed out a hotel master key at the front desk as he did every day at work. Since appellant was not due to clean the hotel banquet rooms until 10:00 a .m., he began to help Metcalfe set up the complimentary breakfast area. Shortly after 6:00 a.m., appellant learned that a coworker would not be in to work that morning, so he went to the

second floor of the hotel to begin cleaning the banquet rooms. Appellant stated that at around that time, he slipped on steps outside the hotel and fell, cutting his left hand while taking trash out to the hotel dumpster. He then finished cleaning the Maple banquet room and went downstairs to help with the hotel's complimentary breakfast.

According to Lilley, appellant was forceful and almost defensive when he claimed that he worked at the breakfast from approximately 6:30 a.m. to 8:00 a.m. that day. Appellant further claimed that he was cleaning tables in the restaurant dining area when he heard screams from the second floor as well as a trouble call over a coworker's employer-provided walkie-talkie.

Appellant told Lilley that he again hurt his hand in a banquet room later that day and that he really thought nothing more of the injury until it started bothering him several days later on September 6. Appellant reiterated that he never left the restaurant on September 3 between 6:30 and 8:00 a.m. and asserted that he was never inside Room 237, since he had no reason to be in any of the guest rooms at the hotel. Lilley asked if he was involved in the murder, and appellant declared that he wanted to talk to an attorney before he answered any more questions. At that point, the interview ceased.

The police secured Metcalfe's consent to search her residence and also obtained a warrant to search a vehicle owned by appellant, which was parked in Metcalfe's driveway in Loveland. In addition, police obtained a search warrant for appellant's residence on Morman Avenue in Cincinnati. While police seized many items of apparel from the two residences, none of them yielded any trace evidence of blood. However, the search of appellant's car produced several items of evidence. Inside the toolbox in the trunk of appellant's car was the unique pendant belonging to Nathan. Also recovered from the toolbox was a master key to the hotel, which could open Room 237, where the murder took place. Police also recovered door security chains, which were later used in attempting to match marks on Nathan's body found on autopsy photos.

The last test results on the seized items came back in August 1995, and the case was later submitted to the grand jury. On September 27, 1995, the grand jury indicted appellant on two counts of aggravated felony-murder (during an aggravated burglary and during an aggravated robbery), and separate counts of aggravated burglary and aggravated robbery. Death-penalty specifications attached to each aggravated murder count alleged that appellant was the principal offender in the aggravated murder during a burglary and the principal offender in the aggravated murder during a robbery or committed the offenses with prior calculation and design. Ultimately the prosecution proceeded only on the first alternative, that appellant was the principal offender. R.C. 2929.04(A)(7). Police arrested appellant at his place of employment in downtown Cincinnati later that day and took him to the District 1 police station for processing.

***4** While at the District 1 headquarters, appellant was shown a copy of the indictment and told he was under arrest for the murder of Rhoda Nathan, as well as for burglary and the robbery involving her pendant necklace. At that point, appellant inquired, "What necklace?" Sgt. Lilley then produced a photo sheet of the pendant recovered from the appellant's car and placed it on the table. Appellant then stated that he had never seen it before in his life. Sgt. Lilley told appellant that the pendant had been recovered from the trunk of his car. Appellant declared, "Not in my fucking car."

A jury trial was held wherein numerous witnesses were called by both the prosecution and defense. Among the prosecution witnesses was Dr. John McDonough, who was appellant's physician during his hand surgery. Dr. McDonough testified that he took a culture from the wound in appellant's left hand and that testing indicated a "mixed flora" of organisms. One of the organisms detected was *eikenella corrodens,* an organism usually found in dental plaque, which Dr. McDonough described as extremely rare in hand injuries. Dr. McDonough testified that, within a reasonable degree of medical certainty, the infection to appellant's hand was caused by a fist-tomouth injury because of the presence of *eikenella corrodens*. This type of injury is sometimes referred to as a "fight bite." The defense put into evidence the testimony of an expert, Dr. Joseph Solomkin, who questioned the likelihood of Dr. McDonough's conclusion. Dr. Solomkin testified that it was possible that the *eikenella corrodens* had come from some source other than an assault victim's mouth.

After deliberation, the jury found appellant guilty as charged. At the mitigation hearing, appellant maintained his innocence and refused to allow defense

> counsel to present any mitigation witnesses. Appellant permitted counsel to argue only residual doubt on his behalf at the mitigation hearing. The trial judge specifically asked, "Mr. Jones, is that accurate, sir?" Appellant replied, "Yes, it is, Your Honor."
>
> The defense requested an instruction on residual doubt, but the court refused to instruct based on *State v. Garner* (1995), 74 Ohio St.3d 49, 56–57, 656 N.E.2d 623, 632, which held that a defendant is not entitled to an instruction identifying residual doubt as a mitigating factor.
>
> The jury recommended death, and the court adopted the jury's death-sentence recommendation. At his sentencing hearing, appellant indicated that he twice refused to plead guilty to a charge of manslaughter and that he did not kill Nathan.

State v. Jones, 90 Ohio St.3d 403, 403–406, 739 N.E.2d 300, 305–308 (2000).

In his December 8, 1997, direct appeal to the Court of Appeals of Ohio, First District, Hamilton County, Jones raised eighteen assignments of error which are set out verbatim in the Appendix to this Report.

After reviewing the assignment of errors on the merits, re-weighing the aggravating circumstances against the mitigating factors, and independently assessing the appropriateness of the penalty of death, the court of appeals affirmed Jones's conviction and the sentence of death. *State v. Jones,* 1998 WL 542713 (Ohio App. 1st Dist.1998.).

***5** Jones then appealed to the Ohio Supreme Court, pleading twenty-six propositions of law which are also set forth verbatim in the Appendix to this Report. After reviewing the merits of Jones's propositions of law, re-weighing the aggravating circumstances against the mitigating factors, and independently assessing the appropriateness of the penalty of death, the Ohio Supreme Court affirmed the conviction and death sentence. *State v. Jones,* 90 Ohio St.3d 403, 739 N.E.2d 300 (2000).

Jones then filed an application to reopen his direct appeal under Ohio R.App. P. 26(B) claiming ineffective assistance of appellate counsel in the omission of thirteen new assignments of error. (Return of Writ, Doc. No. 16, Apx. Vol. XV at 18–37.) (As to the contents of the omitted assignments of error, see the Tenth Ground for Relief.) The application was denied on the merits by the Hamilton County Court of Appeals on April 9, 1999. (Return of Writ, Doc. No. 16, Apx. Vol. XV at 191–192); *State v. Jones,* Hamilton Co.App. No. C–970043. He appealed this decision to the Ohio Supreme Court which affirmed the denial on the merits. (Return of Writ, Doc. No. 16, Apx. Vol. XVI at 173); *State v. Jones,* 91 Ohio St.3d 376, 745 N.E.2d 421 (2001).

Jones filed his petition for post-conviction relief under Ohio Revised Code § 2953.21 in the Hamilton County Court of Common Pleas, pleading twenty-nine claims for relief as set forth verbatim in the Appendix to this Report. The trial court denied Jones's Petition for Post–Conviction Relief. (Return of Writ, Doc. No. 16, Apx. Vol. XII at 371–386, "Findings of Fact, Conclusions of Law and Entry Dismissing Petition to Vacate" Hamilton County, Case No. B–9508578, October 25, 1999.) The court of appeals affirmed the decision of the court of common pleas. *State v. Jones,* 2000 WL 1886307 (Ohio App. 1st Dist.2000). Jones then appealed to the Ohio Supreme Court which declined review. (Return of Writ, Doc. No. 16, Apx. Vol. XIV at 151, *State v. Jones,* 91 Ohio St.3d 1510, 746 N.E.2d 612 (2001).

Proceedings in this Court

Jones filed his Notice of Intention to seek habeas relief in this Court on August 24, 2001 (Doc. No. 1), and followed with the Petition on November 26, 2001 (Doc. No. 15). Jones pleads fourteen grounds for relief as follows:

First Ground for Relief

> Juror misconduct during Mr. Jones's capital sentencing hearing denied him a fair and impartial determination of his sentence in violation of the Fifth, Sixth, Eighth, and Fourteenth Amendments to the Constitution of the United States.

Second Ground for Relief

> Prosecutors introduced improper evidence and used improper arguments throughout Mr. Jones's trial. Defense counsel frequently failed to object to the prosecutors' improper tactics; they failed to challenge some constitutionally infirm evidence with a motion

to suppress; and they permitted prejudicial attacks on Mr. Jones's character, going so far as to impugn their own client's character with inadmissible evidence. Throughout the pre-trial and trial proceedings, the trial court failed to ensure that only constitutionally fair and reliable evidence was admitted and arguments made. As a result, Mr. Jones's constitutional rights to effective assistance of counsel, a fair trial, and to be free from an arbitrary and capricious death sentence were violated.

Third Ground for Relief

*6 The fairness of Mr. Jones's trial and the reliability of his convictions and death sentence were undermined by the absence of exculpatory and impeachment evidence that the prosecution should have disclosed. In the alternative, defense counsel were ineffective for failing to discover the exculpatory and impeachment evidence.

Fourth Ground for Relief

Mr. Jones's defense counsel were ineffective when they failed to adequately investigate and prepare to confront state's witness, Dr. McDonough, and when they failed to effectively prepare their own expert, Dr. Solomkin, regarding Mr. Jones's hand injury and the nature of *Eikenella Corrodens.*

Fifth Ground for Relief

Mr. Jones's trial counsel violated his right to effective assistance of counsel by failing to effectively investigate, discover, research, and utilize exculpatory and impeachment evidence and legal arguments which would have seriously undermined the prosecution's ability to carry its burden of proof and procure a death sentence.

Sixth Ground for Relief

Elwood Jones was denied the right to counsel when Attorney Sanks abdicated his role as defense counsel.

Seventh Ground for Relief

Mr. Jones's constitutional right to a fair, non-arbitrary and reliable capital sentencing hearing were violated by his counsel's failure to investigate mitigation evidence and the trial court's refusal to permit the presentation of a viable "residual doubt" mitigation argument.

Eighth Ground for Relief

Systematic flaws in Hamilton County's methods for selecting grand jurors, grand jury forepersons, and petit jury venires yielded racial, gender, and socio-economic biases inimical to Mr. Jones's constitutional rights. His rights were further violated when the prosecution excluded all African–Americans from his jury. Mr. Jones's counsel failed to effectively challenge these unconstitutional systemic factors; failed to raise an obvious challenge; failed to conduct an effective voir dire; and failed to raise effective challenges to venire persons.

Ninth Ground for Relief

Multiple errors in the jury instructions at both phases of Mr. Jones's trial violated his constitutional rights to a fair trial, effective assistance of counsel, and to be free from an arbitrary and capricious death sentence.

Tenth Ground for Relief

Mr. Jones's appellate counsel violated his right to effective assistance of appellate counsel by failing to raise obvious errors, which if raised, would have rendered his conviction and death sentence unreliable. These constitutional violations rendered Mr. Jones's conviction and death sentence unreliable.

Eleventh Ground for Relief

Elwood Jones is innocent.

Twelfth Ground for Relief

The proportionality review that the appellate courts must conduct pursuant to Ohio Rev.Code § 2929.05 is fatally flawed. Therefore, Elwood Jones's death sentence must be vacated pursuant to the Fifth, Eighth, and Fourteenth Amendments to the United States Constitution.

Thirteenth Ground for Relief

*7 Elwood Jones's death sentence is constitutionally infirm because Ohio's capital punishment system operates in an arbitrary, capricious, and discriminatory manner in violation of the Fifth, Sixth, Eighth, and Fourteenth Amendments.

Fourteenth Ground for Relief

The cumulative effects of the errors and omissions presented in this habeas petition constitute constitutional violations which merit relief.
(Petition, Doc. No. 15.) On Motion to Amend (Doc. No. 142), Jones was permitted to add the following to Ground Three:

> The Government violated its obligation under *Napue v. Illinois,* 360 U.S. 264, 79 S.Ct. 1173, 3 L.Ed.2d 1217 (1959); *Brady v. Maryland,* 373 U.S. 83, 83 S.Ct. 1194, 10 L.Ed.2d 215 (1963); *Giglio v. United States,* 405 U.S. 150, 92 S.Ct. 763, 31 L.Ed.2d 104 (1972); and *Kyles v. Whitley,* 514 U.S. 419, 115 S.Ct. 1555, 131 L.Ed.2d 490 (1995); by failing to disclose evidence favorable to the defense.

Respondent Bagley, Warden of the Mansfield Correctional Institute, filed a Return of Writ on January 7, 2002, asking this Court to deny Jones's Petition for Writ of Habeas Corpus. (Return of Writ, Doc. No. 16.) In response, Petitioner filed a Traverse on September 6, 2006, and an amended Traverse on September 7, 2006, and November 14, 2007(Doc. Nos. 77, 79, and 144), see also (Letter by counsel regarding Post–Hearing Amended Traverse, Doc. No. 154.)
Discovery was granted and an evidentiary hearing was held on the third, fourth, fifth, and tenth grounds for relief on September 24–25, 2007 (See Doc. Nos. 24, 33, 43, Order Granting Motion for Discovery, October 6, 2005, Doc. No. 103; Evid Hrg. Tr. 9/24/07, Doc. Nos. 132, 133) The parties then briefed the merits. (Traverse, Doc. No. 144); (Respondent's Post–Evidentiary Hearing Brief, Doc. No. 147); (Jones's Reply Memorandum in Support of Post–Hearing Traverse, Doc. No. 149); (Letter by counsel regarding Petitioner's Post–Hearing Brief, Doc. No. 153.)

Standard of Review and Generally Applicable Law

The AEDPA

The Antiterrorism and Effective Death Penalty Act ("AEDPA") became effective April 24, 1996. As Jones's petition was filed thereafter, it is subject to its provisions. 28 U.S.C. § 2254, as amended by the AEDPA, provides:

> (d) An application for a writ of habeas corpus on behalf of a person in custody pursuant to the judgment of a State court shall not be granted with respect to any claim that was adjudicated on the merits in state court proceedings unless the adjudication of the claim-
>
> (1) resulted in a decision that was contrary to, or involved an unreasonable application of, clearly established federal law, as determined by the Supreme Court of the United States; or
>
> (2) resulted in a decision that was based on an unreasonable determination of the facts in light of the evidence presented in the State court proceeding.
>
> (e) (1) In a proceeding instituted by an application for a writ of habeas corpus by a person in custody pursuant to the judgment of a State court, a determination of a factual issue made by a State court shall be presumed to be correct. The applicant shall have the burden of rebutting the presumption of correctness by clear and convincing evidence.

***8** Under AEDPA, any factual finding made by the state courts is presumed to be correct and a petitioner must rebut the presumption of correctness by clear and convincing evidence. 28 U.S.C. § 2254(e). A state court's decision is contrary to the Supreme Court's clearly-established precedent if (1) the state court applies a rule that contradicts the governing law as set forth by the Supreme Court case law, or (2) the state court confronts a set of facts that are materially indistinguishable from those in a decision of the Supreme Court and nonetheless arrives at a result different from Supreme Court precedent. *Terry Williams v. Taylor,* 529 U.S. 362, 405–06, 120 S.Ct. 1495, 146 L.Ed.2d 389 (2000). A state court's decision involves an unreasonable application of clearly established federal law "if the state court identifies the correct governing legal rule [from the Supreme Court] but unreasonably applies it to the facts of the particular state prisoner's case," "if the state court either unreasonably extends a legal principle from [Supreme Court] precedent to a new context where it should not apply[,] or [if the state court] unreasonably refuses to extend that principle to a new context where it should apply." *Williams,* 529 U.S. at 407–08. See also *Brown v. Payton,* 544 U.S. 133, 134, 125 S.Ct. 1432, 161 L.Ed.2d 334 (2005); *Bell v. Cone,* 535 U.S. 685, 693–94, 122 S.Ct. 1843, 152 L.Ed.2d 914 (2002); *Nields*

v. Bradshaw, 482 F.3d 442, 449 (6th Cir.2007); *Benge v. Johnson,* 474 F.3d 236, 241 (6th cir.2007).

Procedural Default

The standard for evaluating a procedural default defense is as follows:

> In all cases in which a state prisoner has defaulted his federal claims in state court pursuant to an adequate and independent state procedural rule, federal habeas review of the claims is barred unless the prisoner can demonstrate cause of the default and actual prejudice as a result of the alleged violation of federal law; or demonstrate that failure to consider the claims will result in a fundamental miscarriage of justice.

Coleman v. Thompson, 501 U.S. 722, 749, 111 S.Ct. 2546, 115 L.Ed.2d 640 (1991); *see also Simpson v. Jones,* 238 F.3d 399, 406 (6th Cir.2000). That is, a petitioner may not raise on federal habeas a federal constitutional right he could not raise in state court because of procedural default. *Wainwright v. Sykes,* 433 U.S. 72, 97 S.Ct. 2497, 53 L.Ed.2d 594 (1977); *Engle v. Isaac,* 456 U.S. 107, 102 S.Ct. 1558, 71 L.Ed.2d 783 (1982). Absent cause and prejudice, a federal habeas petitioner who fails to comply with a State's rules of procedure waives his right to federal habeas corpus review. *Boyle v. Million,* 201 F.3d 711, 716 (6th Cir.2000); *Murray v. Carrier,* 477 U.S. 478, 485 (1986); *Engle v. Isaac,* 456 U.S. 107, 102 S.Ct. 1558, 71 L.Ed.2d 783 (1982); *Wainright v. Sykes,* 433 U.S. 72, 87, 97 S.Ct. 2497, 53 L.Ed.2d 594 (1977). *Wainright* replaced the "deliberate bypass" standard of *Fay v. Noia,* 372 U.S. 391, 83 S.Ct. 822, 9 L.Ed.2d 837 (1963).

Failure to raise a constitutional issue at all on direct appeal is subject to the cause and prejudice standard of *Wainwright v. Sykes,* 433 U.S. 72, 97 S.Ct. 2497, 53 L.Ed.2d 594 (1977). *Murray v. Carrier,* 477 U.S. 478, 485, 106 S.Ct. 2639, 91 L.Ed.2d 397 (1986); *Mapes v. Coyle,* 433 U.S. 72, 413, 97 S.Ct. 2497, 53 L.Ed.2d 594 (6th Cir.1999); *Rust v. Zent,* 17 F.3d 155 (6th Cir.1994); *Leroy v. Marshall,* 757 F.2d 94 (6th Cir.1985). Failure to present an issue to the state supreme court on discretionary review constitutes procedural default. *O'Sullivan v. Boerckel,* 526 U.S. 838, 119 S.Ct. 1728, 144 L.Ed.2d 1 (1999).

***9** The Sixth Circuit Court of Appeals requires a four-part analysis when the State alleges a habeas claim is precluded by procedural default. *Reynolds v. Berry,* 146 F.3d 345, 347–48 (6th Cir.1998), *citing Maupin v. Smith,* 785 F.2d 135, 138 (6th Cir.1986); *accord Lott v. Coyle,* 261 F.3d 594 (6th Cir.2001).

> First the court must determine that there is a state procedural rule that is applicable to the petitioner's claim and that the petitioner failed to comply with the rule.
>
> ....
>
> Second, the court must decide whether the state courts actually enforced the state procedural sanction, *citing County Court of Ulster County v. Allen,* 442 U.S. 140, 149, 99 S.Ct. 2213, 60 L.Ed.2d 777 (1979).
>
> Third, the court must decide whether the state procedural forfeiture is an "adequate and independent" state ground on which the state can rely to foreclose review of a federal constitutional claim.
>
> Once the court determines that a state procedural rule was not complied with and that the rule was an adequate and independent state ground, then the petitioner must demonstrate under *Sykes* that there was "cause" for him to not follow the procedural rule and that he was actually prejudiced by the alleged constitutional error.

Maupin, 785 F.2d at 138.

In all cases in which a state prisoner has procedurally defaulted on his federal claims in state court pursuant to an independent and adequate state procedural rule, federal habeas review is barred unless the prisoner can demonstrate cause for the default and actual prejudice as a result of the alleged violation of federal law, or demonstrate that the petitioner is "actually innocent." *Coleman v. Thompson,* 501 U.S. 722, 749, 111 S.Ct. 2546, 115 L.Ed.2d 640 (1991); *see also Simpson v. Jones,* 238 F.3d 399, 406 (6th Cir.2000).

Attorney error amounting to ineffective assistance of counsel does constitute excusing cause. *Murray v. Carrier,* 477 U.S. 478, 488 (1985); *Howard v. Bouchard,* 405 F.3d 459, 478 (6th Cir.2005); *Lucas v. O'Dea,* 179 F.3d 412, 418 (6th Cir.1999); *Gravley v. Mills,* 87 F.3d 779, 785 (6th Cir.1996). However, the same case holds that the

exhaustion doctrine "generally requires that a claim of ineffective assistance of counsel be presented to the state courts as an independent claim before it may be used to establish cause for a procedural default in federal habeas proceedings." *Murray v. Carrier,* 477 U.S. 478, 489 (1985); *Ewing v. McMackin,* 799 F.2d 1143, 1149–50 (6th Cir.1986). Attorney error cannot constitute cause where the error caused a petitioner to default in a proceeding in which he was not constitutionally entitled to counsel, e.g., a discretionary appeal or state post-conviction proceeding. *Coleman v. Thompson,* 501 U.S. 722, 111 S.Ct. 2546, 115 L.Ed.2d 640 (1991). An ineffective assistance of counsel claim cannot be presented as cause if it was procedurally defaulted in the state courts, unless one of the standard excuses for that procedural default exists, to wit, actual innocence or cause and prejudice. *Edwards v. Carpenter,* 529 U.S. 446, 120 S.Ct. 1587, 146 L.Ed.2d 518 (2000), *overruling Carpenter v. Mohr,* C–2–96–447 (S.D.Ohio, 1997), aff'd., 163 F.3d 938 (6th Cir.1998). State court determinations of ineffective assistance of counsel claims are entitled to AEDPA deference in federal habeas corpus, whether those claims are offered as claims for relief in their own right in habeas or as excusing cause for a procedural default.

***10** To meet the "actual innocence" standard, the petitioner must demonstrate that "it is more likely than not that no reasonable fact finder would have found petitioner guilty beyond a reasonable doubt" or "must show by clear and convincing evidence that, but for a constitutional error, no reasonable juror would have found the petitioner eligible for the death penalty under the applicable state law." *Schlup v. Delo,* 513 U.S. 298, 115 S.Ct. 851, 130 L.Ed.2d 808 (1995) (articulating the necessary standard to prove actual innocence of the crime in which the petitioner was convicted); *Sawyer v. Whitley,* 505 U.S. 333, 336, 350, 112 S.Ct. 2514, 120 L.Ed.2d 269 (1992) (setting forth standard which applies the *Schlup* "actual innocence" standard to the sentencing phase of the trial.)

Prosecutorial Misconduct

On habeas corpus review, the standard to be applied to claims of prosecutorial misconduct is whether the conduct "so infected the trial with unfairness as to make the resulting conviction a denial of due process, *Donnelly v. DeChristoforo,* 416 U.S. 637, 643, 94 S.Ct. 1868, 40 L.Ed.2d 431 (1974); *Darden v. Wainwright,* 477 U.S. 168, 106 S.Ct. 2464, 91 L.Ed.2d 144 (1986); *Bates v. Bell,* 402 F.3d 635, 640–41 (6th Cir.2005); *Kincade v. Sparkman,* 175 F.3d 444 (6th Cir.1999) or whether it was "so egregious as to render the entire trial fundamentally unfair." *Cook v. Bordenkircher,* 602 F.2d 117 (6th Cir.1979); accord *Summitt v. Bordenkircher,* 608 F.2d 247 (6th Cir.1979), *aff'd sub nom, Watkins v. Sowders,* 449 U.S. 341, 101 S.Ct. 654, 66 L.Ed.2d 549 (1981); *Stumbo v. Seabold,* 704 F.2d 910 (6th Cir.1983). The court must first decide whether the complained-of conduct was in fact improper. *Frazier v. Huffman,* 343 F.3d 780 (6th Cir.2003), *citing United States v. Carter,* 236 F.3d 777, 783 (6th Cir.2001). A four-factor test is then applicable to any conduct the Court finds inappropriate: "(1) whether the conduct and remarks of the prosecutor tended to mislead the jury or prejudice the defendant; (2) whether the conduct or remarks were isolated or extensive; (3) whether the remarks were deliberately or accidentally made; and whether the evidence against the defendant was strong." *Id.* The court must decide whether the prosecutor's statement likely had a bearing on the outcome of the trial in light of the strength of the competent proof of guilt. *Angel v. Overberg,* 682 F.2d 605, 608 (6th Cir.1982). The court must examine the fairness of the trial, not the culpability of the prosecutor. *Serra v. Michigan Department of Corrections,* 4 F.3d 1348, 1355 (6th Cir.1993) (quoting *Smith v. Phillips,* 455 U.S. 209, 219, 102 S.Ct. 940, 71 L.Ed.2d 78 (1982). In *Serra,* the Sixth Circuit identified factors to be weighed in considering prosecutorial misconduct:

> In every case, we consider the degree to which the remarks complained of have a tendency to mislead the jury and to prejudice the accused; whether they are isolated or extensive; whether they were deliberately or accidentally placed before the jury, and the strength of the competent proof to establish the guilt of the accused.

***11** *Id.,* at 1355–56 (quoting Angel, 682 F.2d at 608). The misconduct must be so gross as probably to prejudice the defendant. *Prichett v. Pitcher,* 117 F.3d 959, 964 (6th Cir.1997), *cert. denied,* 522 U.S. 1001, 118 S.Ct. 572, 139 L.Ed.2d 411 (1997); *United States v. Ashworth,* 836 F.2d 260, 267 (6th Cir.1988). Claims of prosecutorial misconduct are reviewed deferentially on habeas review. *Thompkins v. Berghuis,* 547 F.3d 572 (6th Cir.2008), citing *Millender v. Adams,* 376 F.3d 520, 528 (6th Cir.2004).

Ineffective Assistance of Counsel

The general governing standard for effective assistance of counsel is found in *Strickland v. Washington,* 466 U.S. 668, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984):

> A convicted defendant's claim that counsel's assistance was so defective as to require reversal of a conviction or death sentence has two components. First, the defendant must show that counsel's performance was deficient. This requires showing that counsel was not functioning as the "counsel" guaranteed the defendant by the Sixth Amendment. Second, the defendant must show that the deficient performance prejudiced the defense. This requires showing that counsel's errors were so serious as to deprive the defendant of a fair trial, a trial whose result is reliable. Unless a defendant makes both showings, it cannot be said that the conviction or death sentence resulted from a breakdown in the adversary process that renders the result unreliable.

466 U.S. at 687.

With respect to the first prong of the *Strickland* test, the Supreme Court has commanded:

> Judicial scrutiny of counsel's performance must be highly deferential.... A fair assessment of attorney performance requires that every effort be made to eliminate the distorting effects of hindsight, to reconstruct the circumstances of counsel's challenged conduct, and to evaluate the conduct from counsel's perspective at the time. Because of the difficulties inherent in making the evaluation, a court must indulge a strong presumption that counsel's conduct falls within a wide range of reasonable professional assistance; that is, the defendant must overcome the presumption that, under the circumstances, the challenged action "might be considered sound trial strategy."

466 U.S. at 689.

As to the second prong, the Supreme Court held:

> The defendant must show that there is a reasonable probability that, but for counsel's unprofessional errors, the result of the proceeding would have been different. A reasonable probability is a probability sufficient to overcome confidence in the outcome.

466 U.S. at 694; *see also Darden v. Wainright,* 477 U.S. 168, 106 S.Ct. 2464, 91 L.Ed.2d 144 (1986); *Wong v. Money,* 142 F.3d 313, 319 (6th Cir.1998); *Blackburn v. Foltz,* 828 F.2d 1177 (6th Cir.1987); *see generally* Annotation, 26 ALR Fed 218.

A criminal defendant is entitled to effective assistance of counsel on appeal as well as at trial, counsel who acts as an advocate rather than merely as a friend of the court. *Evitts v. Lucey,* 469 U.S. 387, 105 S.Ct. 830, 83 L.Ed.2d 821 (1985); *Penson v. Ohio,* 488 U.S. 75, 109 S.Ct. 346, 102 L.Ed.2d 300 (1988). Counsel must be appointed on appeal of right for indigent criminal defendants. *Douglas v. California,* 372 U.S. 353, 83 S.Ct. 814, 9 L.Ed.2d 811 (1963); *Anders v. California,* 386 U.S. 738, 87 S.Ct. 1396, 18 L.Ed.2d 493 (1967); *United States v. Cronic,* 466 U.S. 648, 104 S.Ct. 2039, 80 L.Ed.2d 657 (1984). The right to counsel is limited to the first appeal as of right. *Ross v. Moffitt,* 417 U.S. 600, 94 S.Ct. 2437, 41 L.Ed.2d 341 (1974); *Lopez v. Wilson,* 426 F.3d 339 (6th Cir.2005). The *Strickland* test applies to appellate counsel. *Burger v. Kemp,* 483 U.S. 776, 107 S.Ct. 3114, 97 L.Ed.2d 638 (1987). The attorney need not advance every argument, regardless of merit, urged by the appellant. *Jones v. Barnes,* 463 U.S. 745, 751–52, 103 S.Ct. 3308, 77 L.Ed.2d 987 (1983) ("Experienced advocates since time beyond memory have emphasized the importance of winnowing out weaker arguments on appeal and focusing on one central issue if possible, or at most on a few key issues"). Effective appellate advocacy is rarely characterized by presenting every non-frivolous argument which can be made. *See Smith v. Murray,* 477 U.S. 527, 106 S.Ct. 2661, 91 L.Ed.2d 434 (1986). However, failure to raise an issue can amount to ineffective assistance. *McFarland v. Yukins,* 356 F.3d 688 (6th Cir.2004), *citing Joshua v. Dewitt,* 341 F.3d 430, 441 (6th Cir.2003); *Lucas v. O'Dea,* 179 F.3d 412, 419 (6th Cir.1999); *Mapes v. Coyle,* 171 F.3d 408, 427–29 (6th Cir.1999).

***12** "In order to succeed on a claim of ineffective assistance of appellate counsel, a petitioner must show errors so serious that counsel was scarcely functioning as counsel at all and that those errors undermine the reliability of the defendant's convictions." *McMeans v. Brigano,* 228 F.3d 674 (6th Cir.2000), *citing Strickland,* 466 U.S. 668, 104 S.Ct. 2052, 80 L.Ed.2d 674; and *Rust v. Zent,* 17 F.3d 155, 161–62 (6th Cir.1994). Counsel's failure to raise an issue on appeal could only be ineffective assistance if there is a reasonable probability that inclusion of the issue would have changed the result of the appeal. *McFarland v. Yukins,* 356 F.3d 688 (6th Cir.2004), *citing Greer v. Mitchell,* 264 F.3d 663, 676 (6th Cir.2001), *cert. denied,* 535 U.S. 940, 122 S.Ct. 1323, 152 L.Ed.2d 231 (2002). "Counsel's performance is strongly presumed to be effective." *McFarland,* 356 F.3d at 710, *quoting Scott v. Mitchell,* 209 F.3d 854, 880 (6th Cir.2000) (*citing Strickland*).

ANALYSIS

First Ground for Relief

> Juror misconduct during Mr. Jones's capital sentencing hearing denied him a fair and impartial determination of his sentence in violation of the Fifth, Sixth, Eighth, and Fourteenth Amendments to the Constitution of the United States.

In his first ground for relief Jones argues that his rights were violated as a result of jury misconduct. (Petition, Doc. No. 15 at 21.) Specifically, he argues that extra-judicial evidence, the Bible, was introduced to the jurors in an effort to influence their deliberations during the sentencing phase. *Id.* This ground for relief has been withdrawn. (Traverse, Doc. No. 144 at 42.)

Second Ground for Relief

> Prosecutors introduced improper evidence and used improper arguments throughout Mr. Jones's trial. Defense counsel frequently failed to object to the prosecutors' improper tactics; they failed to challenge some constitutionally infirm evidence with a motion to suppress; and they permitted prejudicial attacks on Mr. Jones's character, going so far as to impugn their own client's character with inadmissible evidence. Throughout the pre-trial and trial proceedings, the trial court failed to ensure that only constitutionally fair and reliable evidence was admitted and arguments made. As a result, Mr. Jones's constitutional rights to effective assistance of counsel, a fair trial, and to be free from an arbitrary and capricious death sentence were violated.
>
> A. Improper Evidence Admitted and Testimony Adduced During Trial
>
> 1. The fact that Mr. Jones exercised his right to counsel was improperly admitted to make him look guilty.
>
> 2. The fact that the Grand Jury indicted Mr. Jones was improperly admitted to make him look guilty.
>
> 3. The fact that Mr. Jones had prior criminal convictions was improperly admitted to make him look guilty.
>
> 4. Inadmissible and unreliable medical opinions and other evidence related to Mr. Jones's hand injury was admitted.
>
> 5. Inadmissible and unreliable evidence was admitted under the guise of "forensic expert testimony" about bruises on Mrs. Nathan's body.
>
> ***13** 6. Defense counsel failed to challenge the use of evidence acquired in violation of Mr. Jones's constitutional right to be free from unlawful searches and seizures.
>
> B. Prosecutors' Improper Closing Argument During the Culpability Phase
>
> C. Prosecutors' Improper Closing Argument During the Mitigation Phase

(Petition, Doc. No. 15 at 23.) This Second Ground for Relief combines claims of trial court error, prosecutorial misconduct, and ineffective assistance of trial counsel. The sub-claims are analyzed seriatim, applying the general legal standards set out above that are applicable to such claims, without re-citing the law in each instance.

A. Improper Evidence Admitted and Testimony Adduced During Trial

1. The fact that Mr. Jones exercised his right to counsel was improperly admitted to make him look guilty.

In his first sub-claim Jones alleges that his rights were violated when the fact he exercised his right to counsel was admitted into evidence and was mentioned again in the State's closing argument. (Petition, Doc. No. 15 at 23); (Traverse, Doc. No. 144 at 43–46.)

Respondent argues that the prosecution did not intentionally elicit this information, but rather it logically followed the line of questioning posed to Officer Lilley regarding the interview of Petitioner and Lilley's narrative recount of that interview. (Return of Writ, Doc. No. 16 at 63.) The Warden further argues that because the trial court immediately gave a curative instruction, there was no violation. *Id.* at 63–64.

Jones raised this sub-claim on direct appeal in both the court of appeals and the Ohio Supreme Court and it is therefore before this Court on the merits. The state supreme court held:

> In his ninth proposition of law, appellant asserts that he was prejudiced when the trial court failed to exclude from evidence the portion of the police officer's notes where appellant invoked his right to counsel. Appellant submits that even though the trial court issued a curative instruction, the danger remained that the challenged portion attracted the jury's attention to an improper inference that could be drawn from its admission.
>
> Clearly, it is improper for evidence to be admitted that a defendant invoked his or her right to counsel. See *Doyle v. Ohio* (1976), 426 U.S. 610, 618–619, 96 S.Ct. 2240, 2245, 49 L.Ed.2d 91, 98; *State v. Chinn* (1999), 85 Ohio St.3d 548, 560–561, 709 N.E.2d 1166, 1178. However, after the officer testified that appellant wanted to talk to an attorney, the trial court immediately reminded the jury that anyone has the right to invoke the right to counsel. In addition, the court charged the jury that "[appellant] also has a constitutional right to stop talking to the police and request counsel at any time. * * * The fact that he stopped talking to the police and invoked his right to counsel must not be considered for any purpose."
>
> Juries are presumed to follow the court's instructions, including instructions to disregard testimony. See *State v. Zuern* (1987), 32 Ohio St.3d 56, 61, 512 N.E.2d 585, 590; *State v. Henderson* (1988), 39 Ohio St.3d 24, 33, 528 N.E.2d 1237, 1246; *State v. Loza* (1994), 71 Ohio St.3d 61, 75, 641 N.E.2d 1082, 1100. Any error was rendered harmless by the trial court's curative instructions. We reject appellant's ninth proposition.

***14** *State v. Jones,* 90 Ohio St.3d 403, 414, 739 N.E.2d 300, 313 (2000).

The U.S. Supreme Court has, of course, held that "the use for impeachment purposes of a defendant's silence, at the time of arrest, and after receiving *Miranda* warnings, violates the Due Process Clause of the 14th Amendment." *Doyle v. Ohio,* 426 U.S. 610, 619, 96 S.Ct. 2240, 49 L.Ed.2d 91 (1976). The Sixth Circuit has stated that, "a prosecutor's or witness's remarks constitute comment on a defendant's silence if the manifest intent was to comment on the defendant's silence, or in the absence of such intent, if the character of the remark was such that the jury would naturally and necessarily so construe the remark." *United States v. Peyton,* 2006 U.S.App. LEXIS 13420 at ——21, 2006 WL 1479031 (6th Cir.2006) *citing United States v. Rivera,* 295 F.3d 461, 469 (5th Cir.2002); *United States v. Ursery,* 109 F.3d 1129, 1134 (6th Cir.1997). The analysis of the context of the comment and the likely effect of the court's curative instruction thus involves the consideration of four factors: 1) whether the remark was manifestly intended to reflect on the failure of the defendant to testify; 2) whether the remark was isolated or extensive; 3) whether the case against defendant was otherwise overwhelming; and 4) whether curative instructions were given and when. *United States v. Ursery;* 109 F.3d 1129, 1135 (6th Cir.1997); *United States v. Moore,* 917 F.2d 215, 225 (6th Cir.1990); *United States v. Pearce,* 912 F.2d 159, 164 (6th Cir.1990).

If the comment is found to be error, it is considered "trial court error," error occurring during the presentation of the case to the jury, and not "structural error" requiring reversal *per se. Arizona v. Fulminante,* 499 U.S. 279, 307–308, 111 S.Ct. 1246, 113 L.Ed.2d 302 (1991). This type of error is "amenable to harmless error analysis because it 'may ... be quantitatively assessed in the context of other evidence presented in order to determine [the effect it had on the trial].' " *Brecht v. Abrahamson,* 507 U.S. 619, 637, 113 S.Ct. 1710, 123 L.Ed.2d 353 (1993) *quoting Arizona v. Fulminante,* 499 U.S. 279, 307, 111 S.Ct. 1246, 113 L.Ed.2d 302 (1991). Therefore, to warrant reversal, the error must have had a "substantial and injurious effect or influence in determining the jury's verdict," or in criminal case with a "beyond a reasonable doubt" standard for conviction, "if one cannot say, with fair assurance, ... that

the judgment was not substantially swayed by error, it is impossible to conclude that substantial rights were not affected." *Brecht v. Abrahamson,* 507 U.S. 619, 637, 113 S.Ct. 1710, 123 L.Ed.2d 353 (1993); *Kotteakos v. United States,* 328 U.S. 750, 765, 66 S.Ct. 1239, 90 L.Ed. 1557 (1946).

The first portion of the record cited in Jones's claim is an excerpt from a sidebar prior to Lilley's testimony, and out of the hearing of the jurors:

> Ms. Adams: I don't want to get into an argument now whether his notes are admissible or not, but if they are, there is a sentence right here, the very last sentence, but I don't really want to argue in front of the jury, but should you decide that the notes are admissible I would ask that that sentence be redacted.
>
> ***15** Mr. Tieger: Judge, I really don't see where if a defendant says, I want an attorney now, I don't see the problem with Sergeant Lilley saying, he asked for an attorney and we stopped the questioning.
>
> Ms. Adams: Judge, I think that's a problem.
>
> The Court: I don't think it is.
>
> Ms. Adams: Well, we would move for it to be stricken because I think he's entitled to do that under the Sixth Amendment, but it is an implication of guilt to the jury.
>
> The Court: You're entitled to an instruction, and I'll tell the jury that.

(Trial Tr. Vol. XV at 1331–1332.) There was no further discussion on the matter and the testimony proceeded:

> Witness: Mr Jones then asked me if I was accusing him of being involved in the murder of the lady at the hotel. I asked him if he was involved in her death. He then said that he wanted to talk to an attorney before—
>
> Ms. Adams: Your Honor, we want to renew our objection. The Court: Go ahead. Objection is noted. Go ahead.
>
> Witness: He then said he wanted to talk to an attorney before he answered any more questions, and that was the end of the interview.
>
> Court: All right. Ladies and gentlemen of the jury, there was an objection to the part of the statement where it is alleged that Mr. Jones said that he wanted to talk to a lawyer. I'm permitting you to hear that so that you understand what happened during the course of the interview.
>
> I'm also reminding you that anybody that is the focus of an investigation, or whether they're not the focus of an investigation, has the right to invoke their right to counsel.

(Trial Tr. Vol. XV at 1348–1349.) Later, when instructing the jury at the end of the guilt phase of trial, the judge reiterated that Jones had the constitutional right to counsel:

> Now, it is not necessary that the defendant take the witness stand in his own defense. He has a constitutional right not to testify. He also has a constitutional right to stop talking to the police and request counsel at any time. The fact that the defendant did not testify must not be considered for any purpose. The fact that he stopped talking to the police and invoked his right to counsel must not be considered for any purpose.

(Trial Tr. Vol. XIX at 1831.)

As part of the above sub-claim Petitioner also cites to a reference made in closing by the prosecution that Jones had consulted with an attorney prior to his arrest.

> You know, it's interesting, when Judge West, the defendant's first attorney, testified in this case, and I talked about shortly after the homicide and before the defendant was actually charged or even questioned. The defendant went and retained Mr. West at that time, who was an attorney at that time, to retain him on this case.
>
> And he told you about some things, about sometimes judges do seal these search warrants. It's a proper thing to keep things out of the public eye. But he told you something else very interesting. That once he started representing the defendant and they took his car, was there anything he asked you to do about that car?
>
> ***16** And he said, yes, constantly, to get it back. Wasn't asking him for his clothes. Wasn't asking for his shoes.

> Wasn't really concerned about anything else, but from his own witness the one thing once that car was seized the defendant wants back was that, to get that car back. Fortunately, he was too late.

(Trial Tr. Vol. XIX at 1749.)

The first comment, while informing the jury as to the "interview proceedings," was also an improper comment on Jones's silence, or of such that the character of the remark could be construed by the jury to be a comment on a Jones's silence. However, this error is harmless, as it was an isolated comment, the court immediately gave a curative instruction to the jury that they could not consider Jones's request for an attorney as an admission of guilt, and they were again instructed during jury instructions that it [request for attorney and silence] could not be considered for any purpose. A jury is presumed to follow curative instructions as given by the court. *Richardson v. Marsh,* 481 U.S. 200, 211, 107 S.Ct. 1702, 95 L.Ed.2d 176 (1987). Further, the closing statement was a summary of testimony presented. When considered with the curative instructions and other evidence presented, the comments did not have a substantial effect or influence on the jury's verdict. The comments made the prosecutor, while improper, did not amount to constitutional error, there was no trial court error, nor were defense counsel ineffective. The decision of the state courts on these points is neither contrary to, nor an unreasonable application of United States Supreme Court law, particularly *Doyle, supra.*

2. The fact that the Grand Jury indicted Mr. Jones was improperly admitted to make him look guilty.

In this next sub-claim, Petitioner argues that his indictment by the Grand Jury was improperly admitted in an effort to make him appear guilty. (Petition, Doc. No. 15 at 24.) He alleges that the prosecutor's question to the chief investigating police officer as to why they had waited over a year to arrest Jones elicited testimony that it had gone to the grand jury. (Traverse, Doc. No. 144 at 48.) This comment allegedly gave an improper seal of approval to the State's case in chief. *Id.* Jones further alleges trial counsel's ineffectiveness in their failure to object to this testimony. *Id.*

Respondent counters this claim on the merits by arguing that the State was properly questioning the witness about the investigation and arrest, and that the officer mentioning the indictment was rationally connected to the case. (Return of Writ, Doc. No. 16 at 64 .) Furthermore, the Warden argues, that the jurors were properly instructed by the trial court that "the fact it [the indictment] was filed may not be considered for any purpose." *Id.* In addition, Respondent argues that this sub-claim has not previously been raised and, absent demonstrating cause and prejudice in this failure to raise, the claim is procedurally defaulted. (Return of Writ, Doc. No. 16 at 59–60.)

***17** A failure to raise a constitutional issue at all on direct appeal is subject to the cause and prejudice standard of *Wainwright v. Sykes,* 433 U.S. 72, 97 S.Ct. 2497, 53 L.Ed.2d 594 (1977). *Murray v. Carrier,* 477 U.S. 478, 485, 106 S.Ct. 2639, 91 L.Ed.2d 397 (1986); *Mapes v. Coyle,* 171 F.3d 408, 413 (6th Cir.1999); *Rust v. Zent,* 17 F.3d 155 (6th Cir.1994); *Leroy v. Marshall,* 757 F.2d 94 (6th Cir.1985). Jones attempts to demonstrate cause by arguing the claim was not brought at the proper time as a result of ineffective assistance of appellate counsel and that he raised this claim as an underlying claim in his ineffective assistance of appellate counsel motion under 26(B), Application for Reopening. (Return of Writ, Doc. No. 16, Apx. XV at 18–49); *State v. Murnahan,* 63 Ohio St.3d 60, 584 N.E.2d 1204 (1992).

Respondent argues that Jones did not save the claim from being procedurally defaulted by raising it in the *Murnahan* motion as both the Ohio Court of Appeals and Ohio Supreme Court denied the motion, finding that appellate counsel were not ineffective. (Return of Writ, Doc. No. 16 at 60.) As noted above, this Court reviews state court determinations on ineffective assistance of counsel claims under the deferential AEDPA standard. As to this particular omitted assignment of error, the Ohio Court of Appeals held and indeed all the claims made in the Ohio App. R.:[1]

1 Although the Ohio Supreme Court affirmed denial of the 26(B) motion on the merits, it did so summarily and without explaining its decision. *State v. Jones,* 91 Ohio St.3d 376, 745 N.E.2d 421 (2001). Where there has been one reasoned state court judgment rejecting a federal claim, there is a rebuttable presumption that later unexplained orders upholding the judgment or rejecting the same claim rest on the same ground. *Ylst v. Nunnemaker,* 501 U.S. 797, 111 S.Ct. 2590, 115 L.Ed.2d 706 (1991). The district court must look

> at the last state court disposition providing reasons for the decision. *Couch v. Jabe,* 951 F.2d 94, 96 (6th Cir.1991).
>
> Appellant's application contains thirteen assignments of error. Under each assignment is a list of "issues" which total thirty-four in number. All of the issues except one [footnote omitted] consist of one or more claims of error that allegedly occurred at trial. As the Ohio Supreme Court stated in *State v. McNeill (1998),* 83 Ohio St.3d 457, 459, 700 N.E.2d 613, 615, an allegation of error that occurred at trial "does not allege ineffective assistance of appellate counsel ... [and] therefore [is] not properly raised in an App. R. 26(B) application ....
>
> *State v. Jones,* Case No. C–970043 (Ohio App. 1st Dist. Apr. 9, 1999) (unreported; copy at Apx. Vol. XV, p. 191).

To prevail on a claim of ineffective assistance of appellate counsel, a habeas petitioner must meet the Strickland standard as applied at the appellate level: he or she must show that the omission of a particular assignment of error on appeal fell below accepted professional standards and was also likely to have changed the result of the appeal. The Ohio Court of Appeals and subsequent Ohio Supreme Court determination on the merits of Petitioner's Ohio App. R. 26(B) application, given Petitioner's failure even to attempt to meet those standards, is not contrary to or an objectively unreasonable application of clearly established United States Supreme Court law applying *Strickland* to ineffective assistance of appellate counsel claims.

Therefore, Jones has failed to demonstrate "cause" for his procedural default. (Return of Writ, Doc. No. 16, Apx. XV at 18–49.) He has also failed to make a showing that he was prejudiced by the alleged error, or that his conviction is the result of a fundamental miscarriage of justice. *Id.* Respondent argues that this analysis applies to not only Petitioner's second sub-claim but also the third, fourth, and part of his fifth sub-claim as well. *Id.*

***18** If appellate counsel were found to be ineffective in failing to raise these claims, that could constitute "cause, excusing Petitioner's failure to raise them on direct appeal." Of course, a claim of ineffective assistance of appellate counsel can itself be procedurally defaulted by failing to present it properly to the state courts. *Edwards v. Carpenter,* 529 U.S. 446, 120 S.Ct. 1587, 146 L.Ed.2d 518 (2000). It is also noted that raising a claim of ineffective assistance of appellate counsel is not the same as properly raising the underlying claim, and does not save the underlying claim from procedural default. *Lott v. Coyle,* 261 F.3d 594 (6th Cir.2001). However, both the state court of appeals and supreme court addressed Jones's 26(B) motion on its merits, so that claim is now properly before this Court for review. As the merits of the ineffective assistance of appellate counsel claim are preserved for this Court's review[2], some examination of the merits of this underlying sub-claim are necessary.

2 Albeit under the deferential AEDPA standard that the state court decision can be reversed only if it is contrary to or an objectively unreasonable application of clearly established United States Supreme Court law.

The testimony in question is reproduced below:

> Q: And on September—I believe 27th of 1995, did the grand jury issue an indictment for aggravated murder, aggravated robbery and aggravated burglary against the defendant?
>
> A: That is correct.
>
> Q: Based on that indictment at around 12:30 or so in the afternoon, what did you do?
>
> A: We knew that Mr. Jones was employed at KD Lamp in the downtown area of Cincinnati. We responded to District 1, asked for the assistance of several Cincinnati District 1 officers, and we went to KD Lamp to affect [sic] the arrest of Mr. Jones.

(Trial Tr. Vol. XV at 1359.)

Comments that are directed to suggest a defendant's guilt merely because he was prosecuted or indicted are improper. *United States v. Polk,* 1999 U.S.App. LEXIS 11414 (6th Cir.1999), *United States v. Leon,* 534 F.2d 667 (6th Cir.1976). Again, in determining whether or not there was prosecutorial misconduct, the court must consider if the comments were flagrant, if they misled the jury or prejudiced the defendant, whether they were isolated or extensive, and finally, whether the comments were made deliberately. *United States v. Brown,* 66 F.3d 124, 127 (6th Cir.1995).

The comment regarding the indictment of Petitioner was an isolated remark and arose during the questioning

of a witness about the chronology of events leading to Petitioner's arrest. (Trial Tr. Vol. XV at 1359.) The comment was not likely to mislead the jury or prejudice Jones as the judge specifically instructed the jurors that an indictment could not be considered:

> The case before you began with the filing of an indictment. The indictment informs the defendant that he has been charged with crimes. The fact that it was filed may not be considered for any purpose. The plea of not guilty is a denial of the charge and puts in issue all the essential elements of the crime or crimes.

(Trial Tr. Vol. XIX at 1826.) A jury is presumed to follow curative instructions as given by the court. *Richardson v. Marsh,* 481 U.S. 200, 211, 107 S.Ct. 1702, 95 L.Ed.2d 176 (1987). The comment did not render Jones's trial fundamentally unfair. Because a claim to the contrary on direct appeal would have been far from a "dead bang winner," the Ohio courts' determination that appellate counsel were not ineffective in their failure to raise this claim on appeal is not objectively unreasonable and therefore entitled to deference. Thus ineffective assistance of appellate counsel cannot serve as "cause" for Jones's failure to bring this claim at the proper time. This sub-claim is procedurally defaulted, and in the alternative, without merit.

3. The fact that Mr. Jones had prior criminal convictions was improperly admitted to make him look guilty.

***19** Next, Jones alleges that his rights were violated when defense counsel, the prosecution, and trial court informed the jury of his prior criminal record, even though he did not testify thereby insulating the jury from hearing about his record under Ohio R. Evid. 609. (Petition, Doc. No. 15 at 24.) Jones elected to have the judge, not the jury, adjudicate the specifications on his indictment that enhanced the potential sentence upon proof of certain types of prior criminal convictions. *Id.* This error was further compounded by the admission of his briefcase into evidence. (Petition, Doc. No. 15 at 25.) He alleges that informing the jury of his past record resulted in trial court error, prosecutorial misconduct, and ineffectiveness of trial counsel. *Id.*

Respondent counters by arguing that this sub-claim was not properly raised on direct appeal and is now procedurally defaulted. (Return of Writ, Doc. No. 16 at 59.) It is further alleged that Jones's attempt to demonstrate "cause" fails, as even if alleged as an ineffective assistance of appellate counsel claim for failing to bring the claim on direct appeal, it does not preserve the underlying claim. *Id.* at 59–60.

This claim was presented to the state courts in post-conviction relief proceedings, where it was held:

D. Tenth Claim—Failure to Object to Briefcase and Contents

> In his tenth claim for relief, Jones contends that his trial counsel were ineffective for failing to object to the admission of Jones's briefcase and its contents. In support of this claim below, Jones proffered the contents of the briefcase and his own affidavit, which stated that there was no reason to inform the jury of his criminal record. He also presented the affidavit of a criminal investigator, who stated that a juror had told him that the jury had reviewed the contents of the briefcase during its sentencing deliberations, that the briefcase contained information about Jones's criminal record, and that, after viewing the contents, three of the five jurors who had not wanted to impose the death penalty changed their votes because they believed that if Jones had committed other crimes, he had also committed the murder at the Embassy Suites Hotel. Last, he presented Adams's affidavit, in which she stated that neither trial counsel had objected to the admission of the briefcase, that they had reviewed the contents of the briefcase one to two months before trial, but that they had not reviewed its contents during the trial or before its admission.
>
> The trial court determined that the claim was barred by *res judicata.* We agree. The evidence of the contents of the brief case was not evidence outside the record. The affidavit of the criminal investigator is not competent evidence. As we have already explained in our discussion of Jones's twenty-second claim, the investigator's affidavit was insufficient to circumvent the *aliunde* rule. The fact that trial counsel failed to object to the admission of the briefcase was in the original trial record. The fact that counsel failed

> again to review the contents of the briefcase during the trial, while evidence outside the record, failed to demonstrate ineffective assistance.

***20** *State v. Jones,* 2000 WL 1886307 at *9–10 (Ohio App. 1st Dist.2000).

F. Fourteenth Claim–Prior Criminal Record

> In his fourteenth claim, Jones argues that trial counsel were ineffective for informing the jury of his prior criminal record and for failing to object when the prosecutor did the same. In the trial court below, Jones provided his own affidavit in which he stated that he had no idea why counsel provided the jury with the information. He also provided Shank's affidavit, which stated that the failure of trial counsel to object fell below an objectively reasonable standard of performance.
>
> The trial court concluded the claim was barred by *res judicata* . We agree. The claim could have been fairly determined on direct appeal without resort to the affidavits.

State v. Jones, 2000 WL 1886307 at *9–10 (Ohio App. 1st Dist.2000).

This claim is procedurally defaulted. Under Ohio law, claims which can be raised and decided on direct appeal are barred by *res judicata* from litigation in post-conviction relief. *State v. Perry,* 10 Ohio St.2d 175, 226 N.E.2d 104 (1967). As held by the Ohio courts, his claim was based on the record and should have been presented in direct appeal. Ohio's criminal *res judicata* doctrine is an adequate and independent state ground of decision.. *Buell v. Mitchell,* 274 F. 3rd 337 (6th Cir.2001); *Coleman v. Mitchell,* 268 F.3d 417 (6th Cir.2001); *Byrd v. Collins,* 209 F.3d 486, 521–22 (6th Cir.2000), *cert. denied* 531U.S. 1082, 531 U.S. 1082, 121 S.Ct. 786, 148 L.Ed.2d 682 (2001); *Rust v. Zent,* 17 F.3d 155, 160–61 (6th Cir.1994); *Van Hook v. Anderson,* 127 F.Supp.2d 899 (S.D.Ohio 2001). It was actually enforced against Petitioner by the Ohio courts in this case.

Mr. Jones also presented these sub-claims as portions of his Motion to Reopen, alleging that failure to raise them on direct appeal constituted ineffective assistance of appellate counsel. Because this Court must determine the merits of the ineffective assistance of appellate counsel claim under the AEDPA deferential standard, some examination of the merits of Jones's underlying sub-claim is necessary.

After reviewing the trial transcript, the Court concludes an important element of the defense was that Jones was unfairly suspected and targeted because he had a past conviction/prior record, while other employees with equal opportunity and means to commit the crime but without past convictions were not considered as possible suspects. This tone was set during voir dire, when both the prosecution and the defense informed the potential jurors of the past record and questioned them on whether or not that would sway their view of the evidence. (Trial Tr. Vol. XI at 463, 474, 530); (Trial Tr. Vol. XII at 711–712, 731, 775–776, 786.) The State in opening reiterated this by stating:

> One of the things they looked at were some of those who may have had a criminal past, and the defense has already told you, Elwood Jones had a series of three or four or a history of aggravated burglary convictions. He was a natural one to look at.

***21** (Trial Tr. Vol. XIII at 825–826.)

Defense counsel cross-examined a state witness as to the type of criteria used in creating the list of possible suspects, and again argued their defense of Jones' being improperly targeted in the guilt-phase closing.

> Q: Sergeant Lilley, you said that originally in this case you had three suspects, Dodd, Lackey and Mr. Jones, is that correct?
>
> A: I said that they were all on a suspect list, that's correct.
>
> Q: Were there other people on the list?
>
> A: That's a difficult question to answer. There were people that we wanted to take a look at. It makes it sound as if we had a list that was headed "suspect," which isn't really accurate. But it is fair to say that those were three people that we did want to talk to.
>
> Q: And there were other people?
>
> A: There may have been. I can't think of any right off the top of my head.

Q: Well, you went—Mr. Dodd, Mr. Lackey and Mr. Jones all worked at the hotel at some point or another, correct?

A: That is correct.

Q: And they all three had records?

A: That is correct.

Q: Correct?

A: That's correct.

Q: And that was the basis of your identification of them was based on their records that you had them as suspects to begin with, correct?

A: Yes. We ran a criminal history check on the employees of the hotel.

Q: On every employee?

A: Yes.

Q: So if someone did not have a criminal history, then they were not a suspect, is that correct?

A: If they did not have a criminal history they—if they had a criminal history, then they were moved up in priority as far as the people that we wanted to talk to, that's correct.

Q: Did you have any suspects who did not have a criminal history.

A: I'm not sure I understand the question.

(Trial Tr. Vol. XV at 1362.)

> Sergeant Lilley told you that there was no one, when I asked him if there was anyone without a record who was a suspect. His answer was, I don't understand the question. He understood the question. The problem was they had never looked at anybody who didn't have a record as to whether that person could be a suspect or not. That's why we brought up Bill McCall, not because we think Bill McCall did this, but because he should have been looked at. There were things about his behavior that should have been examined in an investigation such as this of such a major crime. But he wasn't.

(Trial Tr. Vol. XIX at 1756.)

With respect to the first prong of *Strickland,* the Supreme Court has stated:

> Judicial scrutiny of counsel's performance must be highly deferential ... A fair assessment of attorney performance requires that every effort be made to eliminate the distorting effects of hindsight, to reconstruct the circumstances of counsel's challenged conduct, and to evaluate the conduct from counsel's perspective at the time. Because of the difficulties inherent in making the evaluation, a court must indulge a strong presumption that counsel's conduct falls within a wide range of professional assistance, that is, the defendant must overcome the presumption that, under the circumstances, the challenged action "might be considered sound trial strategy."

***22** *Strickland v. Washington,* 466 U.S. at 689. Further, an attorney undoubtedly has a duty to consult with the client regarding "important decisions," including questions of overarching defense strategy. *Florida v. Nixon,* 543 U.S. 175, 125 S.Ct. 551, 160 L.Ed.2d 565 (2004), *citing Strickland,* 466 U.S. at 688. That obligation does not require counsel to obtain defendant's consent to every tactical decision. *Id. citing Taylor v. Illinois,* 484 U.S. 400, 417–418, 108 S.Ct. 646, 98 L.Ed.2d 798 (1988) (holding that an attorney has authority to manage most aspects of the defense without obtaining his client's approval.) Certain decisions regarding the exercise or waiver of basic trial rights cannot be made by the attorney. These include whether to plead guilty, waive a jury, testify in his or her own defense, or take an appeal. *Id. citing Jones v. Barnes,* 463 U.S. 745, 751, 103 S.Ct. 3308, 77 L.Ed.2d 987 (1983); *Wainwright v. Sykes,* 433 U.S. 72, 93, n. 1, 97 S.Ct. 2497, 53 L.Ed.2d 594

Petitioner does not meet the *Strickland* standard in asserting ineffective assistance of counsel on this claim as he has not overcome the presumption that this was trial strategy. He is arguing for an alternative theory of defense, but that does not render counsel ineffective for the theory they did choose.

Jones next alleges that the error was compounded when the prosecution offered, without objection, and the trial court admitted his briefcase into evidence. (Petition, Doc. No. 15 at 25.) He argues that the admission the briefcase was irrelevant, prejudicial, and inadmissible as it contained documents relating to his prior conviction. *Id.* The briefcase in dispute was found by Officer Bray in the trunk of Mr. Jones's car. *Id.* at 26. Defense counsel failed to inspect the contents before permitting it to go back to the juror room. *Id.* Through a post-trial interview with one of the jurors, Kenneth Brewer, it was stated that five jurors changed their minds as to the appropriate sentencing based on the material contained within the briefcase. *Id.* The jurors concluded that "if Mr. Jones committed a similar crime in the past, he was likely to have committed the crime in this case." *Id.* Respondent alleges procedural default on this sub-claim for reasons set forth above.

Ohio Rule of Evidence 606(B)[3] codifies the *aliunde* rule and states that "the verdict of a jury may not be impeached by the evidence of a member of the jury unless foundation for the introduction of such evidence is first laid by competent evidence .... from some other source." *Doan v. Brigano,* 237 F.3d 722, 730 (6th Cir.2001) *quoting State v. Adams,* 141 Ohio St. 423, 48 N.E.2d 861, 863 (1943). This "rule is designed to protect the finality of verdicts and to ensure that jurors are insulated from harassment by defeated parties." *Doan,* 237 F.3d at 730, *quoting State v. Schiebel,* 55 Ohio St.3d 71, 564 N.E.2d 54, 61 (1990). The corresponding Federal Rule of Evidence[4] likewise strives to preserve the finality of jury decisions and protect jurors from harassment:

3 Ohio Rule of Evidence Rule 606(B) states: Upon an inquiry into the validity of a verdict or indictment, a juror may not testify as to any matter or statement occurring during the course of the jury's deliberations or to the effect of anything upon his or any other juror's mind or emotions as influencing him to assent to or dissent from the verdict of indictment or concerning his mental processes in connection therewith. A juror may testify on the question whether extraneous prejudicial information was improperly brought to the jury's attention or whether any outside influence was improperly brought to bear on any juror, only after some outside evidence of that act or event has been presented. However, a juror may testify without the presentation of any outside evidence concerning any threat, any bribe, any attempted threat or bribe, or any improprieties of any officer of the court. His affidavit or evidence of any statement by him concerning a matter about which he would be precluded from testifying will not be received for these purposes.

4 Upon an inquiry into the validity of a verdict or indictment, a juror may not testify as to any matter or statement occurring during the course of the jury's deliberations or to the effect of anything upon that or any other juror's mind or emotions as influencing the juror to assent to or dissent from the verdict or indictment or concerning the juror's mental processes in connection therewith, except that a juror may testify on the question whether extraneous prejudicial information was improperly brought to the jury's attention or whether any outside influence was improperly brought to bear upon any juror. Nor may a juror's affidavit or evidence of any statement by the juror concerning a matter about which the juror would be precluded from testifying be received for there purposes.

***23** Let it once be established that verdicts solemnly made and publicly returned into court can be attacked and set aside on the testimony of those who took part in their publication and all verdicts could be, and many would be, followed by an inquiry in the hope of discovering something which might invalidate the finding. Jurors would be harassed * * * in an effort to secure from them evidence of facts which might establish misconduct sufficient to set aside a verdict. If evidence thus secured could be thus used, the result would be to make what was intended to be a private deliberation, the constant subject of public investigation; to the destruction of all frankness and freedom of discussion and conference.

McDonald v. Pless, 238 U.S. 264, 267–268, 35 S.Ct. 783, 59 L.Ed. 1300 (1915).

The affidavit submitted here by Petitioner sets forth information internal to the jury deliberations. It deals specifically with the mind set and behavior of the jurors, how evidence was considered and weighed, and the voting process. As such, the affidavit cannot properly be considered or used to challenge the verdict. Furthermore, even if it were erroneous to admit the briefcase and all its contents, Petitioner cannot demonstrate prejudice. Counsel did in fact go through the briefcase[5] and there were many references at trial to Petitioner's past conviction. The jury had been told during trial that

Petitioner had a past conviction for a similar offense, so any information contained in the briefcase relating to that conviction had already been developed at trial. This claim is procedurally defaulted and the conclusion of the state courts that Petitioner has failed to show ineffective assistance of appellate counsel which might excuse the default is not an objectively unreasonable application of clearly established federal law; in the alternative, the claim is without merit.

5 "I don't remember. I remember the briefcase, when we went to look at all of the evidence at the prosecutor's office. I remember the briefcase because it took forever to go through things and it was a mess. I do not recall it being an admitted exhibit at trial and I can't imagine why it would have been .... I don't, no, I don't remember seeing those [parole papers] in there." (Evid. Trial Tr. 9/25/2007 at 259.)

4. Inadmissible and unreliable medical opinions and other evidence related to Mr. Jones's hand injury was admitted.

Next Petitioner alleges a violation of rights when inadmissible and unreliable medical opinions and other evidence related to his hand injury were admitted. (Petition, Doc. No. 15 at 26.) Specifically he alleges that the testimony from Dr. McDonough regarding *eikenella corrodens* was inadmissible and unreliable and as there were no foundational facts that the victim, Mrs. Nathan, had this bacteria in her mouth. *Id.* at 26–27. As a result the evidence was inadmissible, as was the irrelevant slide show. *Id.* Additionally Petitioner alleges that the State elicited improper double hearsay testimony from Officer Lilley regarding the Petitioner's conversations with Dr. McDonough. *Id.* at 27.

Respondent argues that this sub-claim is procedurally defaulted as it was not properly presented to the state courts; however Respondent also concedes that the sub-claim was presented in Jones's App. R. 26(B) motion. (Return of Writ, Doc. No. 16 at 60.) Upon the same analysis given above, the underlying claim is procedurally defaulted for failure to present unless the Petitioner can demonstrate cause and prejudice. Petitioner alleges ineffective assistance of appellate counsel in an attempt to show cause. (Traverse, Doc. No. 144 at 54.). The Court considers the merits of the ineffective assistance of appellate counsel claim, under the deferential AEDPA standard, to see if cause is demonstrated. Therefore, some examination of the merits of Jones's underlying subclaim is necessary to determine whether his appellate counsel were ineffective for not having raised the claim on direct appeal.

***24** In turning to the merits, this Court agrees with the reasoning of the Respondent. (Return of Writ, Doc. No. 16 at 65.) While the Dr. McDonough did not testify at trial that the victim had tested positive for *eikenella corrodens,* he did however, testify as an expert that Jones's hand wound was infected with *eikenella corrodens,* which is a bacteria naturally occurring in the oral cavity and is "extremely rare" in hand injuries. (Trial Tr. Vol. XIV at 990, 1000.) Dr. McDonough concluded that Jones had injured his hand by striking someone in the mouth. This testimony was rationally connected to the crime because one of Nathan's teeth was discovered loose at the crime scene and another recovered from her stomach. *Id.* Additionally, defense counsel was given an opportunity to fully cross-examine the State's expert witness as well as present testimony from their own expert.

Petitioner alleges error as a result of the slide show presentation by Dr. McDonough. (Trial Tr. Vol. XIV at 994–995.) Defense counsel made a timely objection which was overruled when the State assured the court that the presentation would tie in to Dr. McDonough's testimony in this case. *Id.* at 995. Following the slide show and direct examination, defense counsel wee given a full opportunity to cross-examine Dr. McDonough. *Id.* at 1026. Furthermore, the jury was permitted to assign whatever weight and credibility it deemed appropriate to Dr. McDonough's testimony. Jones has not demonstrated prejudice arising from the slide show presentation or from Dr. McDonough's testimony.

In a sub-claim of similar nature, Petitioner argues that Officer Lilley's testimony on Jones's hand wound was inadmissible as it was double hearsay. (Petition, Doc. No. 15 at 27.) Respondent counters by alleging that Jones fails to show how this evidence was fundamentally unfair. (Return of Writ, Doc. No. 16 at 66.) Additionally, Respondent argues Jones misstates the facts as Officer Lilley did not testify as to what Jones replied when asked by Dr. McDonough if he injured his hand by striking someone in the face. *Id.;* (Trial Tr. Vol. XV at 1336.) Later, however, Officer Lilley did testify that during his own interview of Petitioner, Jones had stated to him that he had never been asked by Dr. McDonough if the injury was a

fight bite. (Return of Writ, Doc. No. 16 at 66); (Trial Tr. Vol. XV at 1347.) Finally, Jones alleges that Officer Lilley improperly characterized him as a liar. (Petition, Doc. No. 15 at 27.) Respondent notes that there was an immediate objection and that the objection was sustained. (Return of Writ, Doc. No. 16 at 66.) Furthermore, the statement was offered, not for the truth of the matter asserted, but to show inconsistencies between the police report and Jones's testimony. *Id.* Therefore, it was not hearsay under Evid. R. 801. *Id.*

Aside from a one sentence assertion that there was double hearsay, Petitioner does little more to advance this claim. He makes no attempt to show that he was prejudiced or that this statement rendered his trial fundamentally unfair. A review of the record shows that Lilley testified that "the information I received was the injury to Mr. Jones' hand was what the doctor referred to as a fist-tomouth injury, so much so that Doctor McDonough asked Mr. Jones if he received the injury by punching someone in the mouth." (Trial Tr. Vol. XV at 1336.) Lilley makes no comment as to Jones's response to Dr. McDonough, as relayed through the doctor. Later, when testifying as to his own interview with Petitioner, Lilley stated that "Mr. Jones said that he was never asked that question by any of the doctors who treated him." (Trial Tr. Vol. XV at 1347 .) Hearsay is defined as a statement other than the one made by a declarant at a trial or hearing that is offered in evidence to prove the truth of the matter asserted. F. Evid. R. 801; Ohio Evid. R. 801. This statement was not offered to prove the truth of the matter asserted, it was admitted to show the steps of the investigation which resulted in the officer obtaining a search warrant, it was not admitted to show whether or not Jones had in fact been asked by the doctor whether or not he had struck someone in the mouth. (Trial Tr. Vol. XV at 1347, 1349–1351.) The Court further notes, that defense counsel objected immediately when Officer Lilley testified that "it was significant to me that Mr. Jones lied ..." (Trial Tr. Vol. XV at 1349.) The trial court sustained this objection. *Id.* When instructing the jurors the judge reminded them that:

> ***25** if a question is asked and an objection to the question was sustained, you did not hear the answer and you must not speculate as to what the answer might have been or as to the reason for the objection. If an answer was given to a question and the Court then granted a motion to strike out the answer, you are to completely disregard such question and answer and not consider them from any purpose. A question in and of itself is not evidence and may be considered by you only as it supplies meaning to the answer.

(Trial Tr. Vol. XIX at 1827–1828.) A jury is presumed to follow curative instructions as given by the court. *Richardson v. Marsh,* 481 U.S. 200, 211, 107 S.Ct. 1702, 95 L.Ed.2d 176 (1987). Regardless, even assuming that any of the above statements had been considered hearsay, Jones is not able to show that he was prejudiced by counsel's ineffectiveness and had they objected the outcome of his trial would have been different. Dr. McDonough testified that he had asked Jones whether or not this was a wound resulting from a human bite and he identified the infection as one being associated with fight-bite type wounds. (Trial Tr. Vol. XIV at 991–994.) Additionally, other evidence of guilt, including finding Ms. Nathan's pendant in Petitioner's locked car trunk, were overwhelming. This sub-claim is procedurally defaulted; and the state courts' determination on the ineffective assistance of appellate counsel claim offered as cause is not an objectively unreasonable application of clearly established federal law.

5. Inadmissible and unreliable evidence was admitted under the guise of "forensic expert testimony" about bruises on Mrs. Nathan's body.

Next Petitioner challenges the forensic expert testimony regarding bruise patterns on the victim's body. (Petition, Doc. No. 15 at 27.) He alleges that the State presented "far less than overwhelming evidence that Mr. Jones murdered Mrs. Nathan." (Petition, Doc. No. 15 at 27.)

Respondent counters by arguing that the admissibility of evidence is left to the discretion of the trial court and that the expert testimony on this subject was reliable and admissible. (Return of Writ, Doc. No. 16 at 80.)

This claim was raised on direct appeal. The Ohio Supreme Court held:

> Under his thirteenth proposition of law, appellant complains that the trial court erred in admitting expert

opinion testimony concerning the correlation between wound patterns on the victim's body and the shape of objects allegedly used in the murder of Nathan. Appellant asserts that the expert opinion testimony of FBI specialist William J. Stokes and Dr. William Oliver of the Armed Forces Institute of Pathology was not based upon widely accepted knowledge, facts, and principles, in violation of Evid. R. 702(C) (1).

In his video deposition, FBI specialist Stokes testified that he used a "rectifying enlarger," the only one he knew of being used for forensic photography, to correct the place of reference scale on autopsy photos of Rhoda Nathan. Stokes explained that the scale on the autopsy photos was not on the same level as the wounds on the victim's body. The rectifying enlarger compensates for perspective by making the wounds on the different plane properly match the scale that is on the autopsy photos. Stokes used State Exhibit 6, a walkie-talkie available to appellant while he was working at the hotel, to help establish the scale of the wounds on the autopsy photo. Stokes then opined that the characteristics of the radio matched up with certain wounds on Nathan's body depicted on State Exhibit 5.

***26** Lieutenant Colonel William Oliver, a medical doctor and forensic pathologist with the Armed Forces Institute of Pathology, also testified in a video deposition. Dr. Oliver was provided autopsy photos of Nathan to evaluate pattern injuries on her body. He converted the photos to digital images to compare certain wounds with physical evidence linked to the homicide, *i.e.*, metal door chains found in appellant's toolbox and the walkie-talkie. Dr. Oliver opined that there was "a correspondence in shape and scale" between the door chains and marks on the victim's body and that he could not rule out "a correspondence" with markings on the victim and the walkie-talkie.

Because neither expert offered an opinion with any reasonable degree of scientific certainty, appellant claims that the testimony should not have been admitted as expert testimony.

Both Stokes and Dr. Oliver were presented as experts in their fields. The standard for determining the admissibility of expert testimony is set forth in Evid. R. 702: whether expert testimony is admissible depends on whether it will assist the trier of fact to understand matters "beyond the knowledge of experience possessed by lay persons." See, generally, *State v. Buell* (1986), 22 Ohio St.3d 124, 129, 22 OBR 203, 207, 489 N.E.2d 795, 801. The state claims that in any event, the opinions were nevertheless admissible, at least as lay witness testimony under Evid. R. 701. See *Jells,* 53 Ohio St.3d at 28–29, 559 N.E.2d at 470–472. In addition, the state cites *State D'Ambrosio* (1993), 67 Ohio St.3d 185, 191, 616 N.E.2d 909–915, where we held that experts could testify as to possibility rather than only probability, and that such testimony becomes an issue of sufficiency and not admissibility.

Agent Stokes's testimony was admissible under Evid. R. 702(C). The comparisons he made between the walkie-talkie and wounds on Nathan's body were similar to techniques used to compare shoeprints and fingerprints in other cases. The reliability of the comparison in this case was in fact called into question by defense counsel during cross-examination. The reliability of Dr. Oliver's conclusions was also effectively challenged on cross-examination when he conceded that he could not say for certain that a walkie-talkie or hotel door chains made the wound markings on Nathan's body.

Since counsel was permitted to fully cross-examine the expert witnesses, and since the trial court properly instructed the jury that they were to decide what weight to give such testimony, no abuse of discretion by the trial court occurred. *Buell,* 22 Ohio St.3d at 132–133, 22OBR at 203, 489 N.E.2d at 803–804. Accordingly, we overrule appellant's thirteenth proposition.

State v. Jones, 90 Ohio St.3d 403, 415–416, 739 N.E.2d 300, 314–315 (2000).

Petitioner argues the State presented four experts, Trimpe, Gerber, Stokes, and Oliver, to render opinions that the bruise patterns on the victim's body were consistent with the physical objects Jones was alleged to have used to beat and stomp the victim to death. (Petition, Doc. No. 15 at 28.) The first problem, however, is that not one of these experts rendered an opinion "to a reasonable degree of scientific certainty", or to any other legal standard, that the objects were used and caused the imprints on the victim. *Id.* The second flaw with their testimony is the absence of foundational facts for the purported opinions rendered. *Id.* This rendered the opinions inadmissible and forced the jury to stack inference upon inference to use this evidence in support of their guilt finding. *Id.* This violated "the fundamental prohibition of drawing inferences from

inferences to 'prove' facts by circumstantial evidence and deprived Mr. Jones of any viable ability to confront this evidence." *Id.* The inferences included that Jones had a walkie-talkie like the one used by the State's experts, that Jones attacked Nathan with it, and that the result of the attack left bruises on the body which matched up with the patterns on the walkie-talkie. *Id.* Thirdly, Petitioner contests that neither Dr. Gerber nor Michael Trimpe were qualified to render expert opinions on the bruise pattern. *Id.* at 29, 739 N.E.2d 300. Likewise, the testimony regarding the blood splatter evidence was also inadmissible. *Id.* Together, the prosecutorial misconduct, ineffective assistance of defense counsel to research and raise proper objections, and trial court error in preventing inadmissible testimony from being presented, violated Petitioner's constitutional rights. *Id.*

***27** Respondent notes that Petitioner is now presenting the inverse of the claim he presented on direct appeal. (Return of Writ, Doc. No. 16 at 67.) There he argued that Stokes and Oliver should *not* be admitted as experts, and now he is arguing that Trimpe and Gerber should have been admitted as experts even though they did not offer such an opinion. *Id.* Jones cannot demonstrate that it was fundamentally unfair that the trial court did not, *sua sponte,* qualified them as experts. *Id.* Additionally Respondent notes that the testimony was rationally connected to Jones's case, it was admissible and reliable. *Id.*

The decision of the state courts was neither contrary to, nor an unreasonable application of federal law. Expert testimony is generally admissible on matters which are not of common knowledge, in which scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue. The court is the "gatekeeper" as to who is an expert and it is the role of the trier of fact to decide, what weight, if any to give the expert opinion testimony. *Sartor v. Arkansas Natural Gas,* 321 U.S. 620, 64 S.Ct. 724, 88 L.Ed. 967 (1944). A trial judge has broad discretion in admitting or excluding expert evidence which is to be sustained unless manifestly erroneous. *United States v. Demjanjuk,* 367 F.3d 623 (6th Cir.2004), *citing United States v. Jones,* 107 F.3d 1147, 1151 (6th Cir.1997). Petitioner has not made a showing that his constitutional rights were violated or that the testimony rendered his trial unfair. Evidentiary questions generally do not rise to the constitutional level unless the error was so prejudicial as to deprive a defendant of a fair trial. *Cooper v. Sowders,* 837 F.2d 284, 286 (6th Cir.1988); *Walker v. Engle,* 703 F.2d 959, 962 (6th Cir.1983); *Bell v. Arn,* 536 F.2d 123 (6th Cir., 1976); *Burks v. Egeler,* 512 F.2d 221, 223 (6th Cir.1975). Where an evidentiary error is so egregious that it results in a denial of fundamental fairness, it may violate due process and thus warrant habeas relief. *Bugh v. Mitchell,* 329 F.3d 496 (6th Cir.2003), *citing Coleman v. Mitchell,* 244 F.3d 533, 542 (6th Cir.2000). Courts have, however, defined the category of infractions that violate fundamental fairness very narrowly. *Bugh, quoting Wright v. Dallman,* 999 F.2d 174, 178 (6th Cir.1993) (*quoting Dowling v. United States,* 493 U.S. 342, 352, 110 S.Ct. 668, 107 L.Ed.2d 708 (1990). "Generally, state-court evidentiary rulings cannot rise to the level of due process violations unless they 'offend[ ] some principle of justice so rooted in the traditions and conscience of our people as to be ranked as fundamental.' " *Seymour v. Walker,* 224 F. 3rd 542, 552 (6th Cir.2000) (*quoting Montana v. Egelhoff,* 518 U.S. 37, 43, 116 S.Ct. 2013, 135 L.Ed.2d 361 (1996)). The Supreme Court has defined very narrowly the category of infractions that violate fundamental fairness. *Bey v. Bagley,* 500 F.3d 514 (6th Cir.2007), *citing Dowling v. United States,* 493 U.S. 342, 352, 110 S.Ct. 668, 107 L.Ed.2d 708 (1990).

***28** Officer Stokes and Dr. Oliver were presented as experts in their fields. Their credibility and the reliability of their findings were subject to cross-examination. The testimony was relevant in that it showed the correlation between objects and marks on the victim's body. Furthermore, the jury was properly instructed that they were to decide on the credibility of the witness and weight of the testimony.

Petitioner alleges that neither Dr. Gerber nor Michael Trimpe was qualified to render expert opinions as to bruise patterns. (Petition, Doc. No. 15 at 29.) This portion of the claim was not raised on direct appeal. Petitioner raised the allegation respecting Trimpe under his ineffective assistance of appellant counsel claim, but made no mention of Gerber. (Petition, Doc. No. 15 at 77.) Again, Petitioner fails to show prejudice. Trimpe offered his opinion that the bruises could have been consistent with the heels of the shoes and with the walkie-talkie radio, but he stated he could not say this to the exclusion of all other shoes and walkie-talkies. (Trial Tr. Vol. 895–897.) He did not testify as an expert witness, but his testimony is permissible under Ohio R. Evid. 701, Opinion Testimony of a Lay Witness. This rule provides that, "[i]f

the witness is not testifying as an expert, the witness' testimony in the form of opinions or inferences is limited to those opinions or inferences which are (a) rationally based on the perception of the witness, and (b) helpful to a clear understanding of the witness' testimony or the determination of a fact in issue." Likewise, the testimony of Detective Alderucci regarding the blood in hotel room was admissible under Rule 701. Here Alderucci was testifying as to his own impression as he observed the blood patterns at the crime scene, it was not based on scientific, technical, or other specialized knowledge. This testimony was not constitutionally impermissible.

6. Defense counsel failed to challenge the use of evidence acquired in violation of Mr. Jones's constitutional right to be free from unlawful searches and seizures.

Petitioner has withdrawn this claim. (Traverse, Doc. No. 144 at 60.)

B. Prosecutors' Improper Closing Argument During the Culpability Phase

C. Prosecutors' Improper Closing Argument During the Mitigation Phase

In his next two sub-claims Petitioner alleges violations resulting from the State's improper arguments made during the closing arguments at both the culpability and the mitigation phases. (Petition, Doc. No. 15 at 31–35); (Traverse, Doc. No. 144 at 60–69.)

As to the culpability portion of this claim, Respondent argues that of the eleven sub-claims, only seven through eleven were properly preserved by being raised in direct appeal. (Return of Writ, Doc. No. 16 at 69.) He argues that the sub-claims are without merit and the decision of the state court was neither contrary to, nor an unreasonable application of clearly established federal law. *Id.* The remaining sub-claims, one through six, are procedurally defaulted as counsel failed to object at trial as required under Ohio's contemporaneous objection rule. (Return of Writ, Doc. No. 16 at 75.) Furthermore, it is alleged that Jones failed to raise these instances of alleged prosecutorial misconduct on direct appeal. *Id.* at 76. Respondent admits Jones did raise these claims in his App. R. 26(B) motion. *Id.* Respondent argues that Jones is unable to show cause and prejudice for failing to raise these arguments during direct appeal. *Id.* As to the mitigation phase, Respondent does not allege procedural default, but rather concedes that all the sub-claims were raised on direct appeal and are preserved for review on the merits. (Return of Writ, Doc. No. 16 at 82.)

***29** For those portions of the claim asserted to be procedurally defaulted portions, this Court must review, under the AEDPA deferential standard, the Ohio courts' determination that omission of those claims on direct appeal did not constitute ineffective assistance of appellate counsel. To do so, the Court must examine to some extent the merits of the underlying claims.

The state supreme court held on direct appeal:

> The test for prosecutorial misconduct is whether remarks were improper and, if so, whether they prejudicially affected substantial rights of the accused. *State v. Smith* (1984), 14 Ohio St.3d 13, 14, 14 OBR 317, 318, 470 N.E.2d 883, 885. The touchstone of analysis "is the fairness of the trial, not the culpability of the prosecutor." *Smith v. Phillips* (1982), 455 U.S. 209, 219, 102 S.Ct. 940, 947, 71 L.Ed.2d 78, 87.
>
> In the first group of comments cited by appellant under his sixth proposition, he claims that the prosecutor improperly appealed to the jurors' passions when he criticized defense counsel for attempting to shift culpability for the murder to other hotel employees: "It's very unfortunate. Their names have been dragged through the mud in front of the cameras, in front of the press, as being accused of murder. A murder that Elwood Jones did." Defense counsel objected, but the court simply instructed the jury: "[Y]ou heard the evidence as well as I did. I'll let you decide what was said about McCall and Henry." The prosecutor's comment appears to be a fair rebuttal to the defense strategy of shifting suspicion of the murder to others who worked at the hotel, and can hardly be characterized as an improper appeal to the jurors' passions.
>
> Appellant also complains that the prosecutor misstated the evidence in asserting that only the banquet department had the kind of walkie-talkie used for comparison to the victim's wounds. Defense counsel's objection was not ruled upon, but one prosecution witness did in fact testify that State Exhibit 6, a walkie-talkie of that kind, was one used by the banquet department, in which appellant worked. Although one defense witness asserted that different departments

at the hotel had walkie-talkies of that kind, the prosecutor's statement was harmless.

Appellant next cites comments where the prosecutor argued that the defense "conceded that a radio made that mark" on the victim's body and where the prosecutor asserted and further intimated that appellant's girlfriend, Earlene Metcalfe, lied for him. Both comments were objected to, and the trial court sustained both objections. However, the prosecutor continued to claim that Metcalfe lied, even though she never testified at trial. In addition, the prosecutor argued that shoes found during the search of her residence belonged to appellant, even though no evidence at trial supported that assertion. We agree with the court of appeals that the comments concerning Metcalfe and the shoes were improper because they alluded to facts not in evidence. However, these isolated comments were not outcome-determinative and did not deprived appellant of a fair trial.

***30** Appellant next argues under his seventh proposition of law that the prosecutor denigrated the role and trial tactics of defense counsel, and suggested that defense counsel were attempting to hide the truth. Here, appellant is referring to the prosecutor's remarks on defense counsel's attempt to cast suspicion for the murder on other hotel employees. During trial, defense counsel elicited testimony from hotel employee Lisa Dietz that another hotel employee, Bill McCall, who left the hotel on the day of the murder, had access to master keys and radios at the hotel. After the defense rested, the state called Bill McCall as a rebuttal witness, and he refused the implication that he had been involved in the murder. During closing argument, the prosecutor commented on defense counsel's "search for doubt, not a search for the truth." This remark, not objected to, was not outcome-determinative and did not deprive appellant of a fair trial.

In addition, appellant points to comments made during the prosecutor's closing argument concerning defense expert Dr. Solomkin's testimony regarding the nature of appellant's hand injury. Defense counsel's objection to the comments was overruled.

Appellant argues that the prosecutor's comments improperly implied that the defense expert would say whatever defense counsel wanted him to say. However, these comments were made during argument. Given the substantial evidence submitted in this case, we find that these isolated comments made during argument were nonprejudicial.

Appellant also claims that the prosecutor misrepresented defense counsel's closing argument during the mitigation phase, and that the defense had "forfeited at this stage of the trial. * * * They are asking you to fill in these blanks that are their mitigation. There is none. They have presented none and now they want you to basically fill in some things for them, to create evidence as it were." However, these comments constituted fair comment by the prosecutor and were neither improper not prejudicial. Appellant chose not to present any mitigation except for residual doubt.

Under his eighth proposition of law, appellant asserts prosecutorial misconduct in the prosecutor's use of the nature and circumstances of the offense as an aggravated circumstance. During the rebuttal closing argument at the mitigation phase, the prosecutor said:

"What is worth more to him at that point, the life of this lady who has absolutely done nothing to him or a trinket? He could have left her alive. What's his choice? Right here. (Indicating)

"And thankfully it was that greed that tripped him up in this case. Had he left [sic] that go, maybe he would have never been caught but he decided at that point and that's the weighing process that he went through. That's the value he put on that lady's life.

"I trust when you weigh that aggravating circumstance you will give Miss Nathan's life more worth than he did."

Defense counsel's objection that the prosecutor was arguing the nature and circumstances of the offense as an aggravating circumstance was overruled. The court of appeals found this statement to be improper and erroneous, but found the comment to be nonprejudicial. This type of prosecutorial argument was directly proscribed in *State v. Wogenstahl* (1996), 75 Ohio St.3d 344, 662 N.E.2d 311, paragraph two of the syllabus.

> ***31** "It is improper for prosecutors in the penalty phase of a capital trial to make any comment before a jury that the nature and circumstances

> of the offense are 'aggravating circumstances.' "
>
> Unlike *Wogenstahl,* the defense attorney did object immediately after the comment was made. The comment violated the law enunciated in *Wogenstahl.* But in view of the entire penalty-phase proceedings, we find the error was harmless. See *State v. Williams* (1983), 6 Ohio St.3d 281, 6 OBR 345, 452 N.E.2d 1323.
>
> In the foregoing consideration, we have found several instances of error that were not outcome-determinative. A similar situation arose in *State v. Lott* (1990), 51 Ohio St.3d 160, 555 N.E.2d 293. In *Lott,* 51 Ohio St.3d at 166, 555 N.E.2d at 301, this court, quoting *United States v. Hasting* (1983), 461 U.S. 499, 508–509, 103 S.Ct. 1974, 1980, 76 L.Ed.2d 96, 106, observed that " 'given the myriad safeguards provided to assure a fair trial, and taking into account the reality of the human fallibility of the participants, there can be no such thing as an error-free, perfect trial, and that the Constitution does not guarantee such a trial. * * * [Citations omitted.] * * *
>
> " ' * * * [I]t is the duty of a reviewing court to consider the trial record as a whole and to ignore errors that are harmless including most constitutional violations.' " In sum, we overrule appellant's fifth, sixth, seventh, and eighth propositions.

State v. Jones, 90 Ohio St.3d 403, 420–422, 739 N.E.2d 300, 318–320 (2000).

Under the standard for evaluating claims of prosecutorial misconduct set out above, the Court must decide whether the prosecutor's statement likely had a bearing on the outcome of the trial in light of the strength of the competent proof of guilt. *Angel v. Overberg,* 682 F.2d 605, 608 (6th Cir.1982). The court must examine the fairness of the trial, not the culpability of the prosecutor. *Serra v. Michigan Department of Corrections,* 4 F.3d 1348, 1355 (6th Cir.1993) *quoting Smith v. Phillips,* 455 U.S. 209, 219, 102 S.Ct. 940, 71 L.Ed.2d 78 (1982). "Even if the prosecutor's conduct was improper or even universally condemned, we can provide relief only if the statements were so flagrant as to render the entire trial fundamentally unfair." *Bowling v. Parker,* 344 F.3d 487, 512 (6th Cir.2003); *Bates v. Bell,* 402 F.3d 635 (6th Cir.2005). Yet reversal is required if the prosecutor's misconduct is "so pronounced and persistent that it permeates the entire atmosphere of the trial or so gross as probably to prejudice the defendant." *Pritchett v. Pitcher,* 117 F.3d 959, 964 (6th Cir.1997); *see also Gall v. Parker,* 231 F.3d 265, 311 (6th Cir.2000), overruled on other grounds by, *Bowling v. Parker,* 344 F.3d 487, 501 n. 3 (6th Cir.2003); *Bates v. Bell,* 402 F.3d 635 (6th Cir.2005). However, *Angel v. Overberg* held "more commonly, ..., the complained of conduct will not rise to the level of reversible error ." This result is particularly true when the conduct is not flagrant, the proof of guilt is overwhelming, counsel does not object, and/or the trial judge cautions the jury. *Angel v. Overberg,* 682 F.2d 605, 607–609 (6th Cir.1982).

***32** Petitioner alleges several instances of prosecutorial misconduct during the closing argument of the culpability phase of his trial. (Petition, Doc. No. 15 at 31.) First he alleges that the State improperly expressed its opinion as to Jones's guilt and vouched for the credibility of the State's case. *Id.* Respondent counters by stating that this claim is procedurally defaulted. Trial counsel failed to make a contemporaneous objection at the time of trial and did not bring the claim during direct appeal. (Return of Writ, Doc. No. 16 at 76.) The claim was brought in Jones's 26(B) motion, but Respondent argues he is unable to show cause to excuse his failure to bring the claim earlier. *Id.* at 69. Additionally, Respondent argues this claim is without merit. *Id.* at 76. The record does not show the prosecutors providing their personal belief as to guilt. (Trial Tr. Vol. XIX at 1793–1794.) This is a comment as to what the evidence showed, not a personal opinion as to belief of Jones's guilt or vouching for the credibility of the case. (Return of Writ, Doc. No. 16 at 78.)

After a review of the record this Court agrees. This claim should have been raised during trial as a contemporaneous objection. It was not, nor was it brought on direct appeal. This sub-claim is procedurally defaulted. However, as it was raised as an underlying claim to support ineffective assistance of appellate counsel, the Court considers the merits in reference to that claim and finds that it is without merit as the closing argument was a commentary on the evidence as opposed to their personal belief of Jones's guilt or vouching for their case.

Next, Jones argues misconduct arising from the statement that he had consulted with counsel before he was questioned by the police. (Petition, Doc. No. 15 at 31); (Traverse, Doc. No. 144 at 62.) Respondent counters by stating that this claim is procedurally defaulted. Trial counsel failed to make a contemporaneous objection and

did not bring the claim during direct appeal. (Return of Writ, Doc. No. 16 at 76.) The claim was brought in Jones's 26(B) Motion, but Respondent argues he is unable to show cause to excuse his failure to bring the claim earlier. *Id.* at 69. Additionally, Respondent alleges this claim is without merit. *Id.* at 78. Respondent concedes that the comment by the prosecutor was improper, but argues the statement did not have a substantial effect or influence on the jury. *Id.*

Because no contemporaneous objection was made and the claim was not raised on direct appeal, it is procedurally defaulted. Petitioner did raise this sub-claim however, as an underlying ground in his ineffective assistance of appellate counsel claim. To the extent necessary to decide that claim, this Court turns to the merits. As discussed earlier the comment made regarding Jones's exercise of his constitutional right was improper. However, because there was an immediate objection and the trial judge instructed the jury multiple times that they could not consider that exercise of his rights for any purpose, the statement was not likely to have had a bearing on the outcome of the trial in light of the strength of the competent proof of guilt. *Angel v. Overberg,* 682 F.2d 605, 608 (6th Cir.1982). This sub-claim is without merit and the state courts' determination that appellate counsel was not ineffective in their failure to raise this claim is not an objectively unreasonable application of federal law.

***33** Next Jones's challenges the comment made in closing that the victim had tested positive for the *eikenella corrodens* bacterium. (Petition, Doc. No. 15 at 31.) Respondent counters by stating that this claim is procedurally defaulted. Trial counsel failed to make a contemporaneous objection at the time of trial and did not bring the claim during direct appeal. (Return of Writ, Doc. No. 16 at 76.) The claim was brought in Jones's 26(B) motion, but Respondent argues he is unable to show cause to excuse his failure to bring the claim earlier. *Id.* at 69. Respondent also argues that even without this comment and the testimony by Dr. McDonough, there is incriminating evidence that Jones murdered Mrs. Nathan. *Id.* at 79.

The State specifically addressed why the victim's teeth had *not* been tested for the *eikenella* bacteria. (Trial Tr. Vol. XIX at 1803.) Later in closing, however, the State argued that it was "very lucky that Rhoda Nathan had the *eikenella* bacteria, because at that point something good came out of something tragic." *Id.* at 1824. Defense counsel did not object to this characterization at the time it was made. Though the statement was improper because it did not refer to actual evidence in the case, it was not likely to have mislead the jury or had a bearing on the outcome of the trial in light of the strength of the competent proof of guilt. *Angel v. Overberg,* 682 F.2d 605, 608 (6th Cir.1982). Neither expert provided testimony that the victim had tested positive for this bacteria. In closing defense counsel thoroughly argued that the victim had *not* been tested and questioned why she had not. (Trial Tr. Vol. XIX at 1777–1778.) In rebuttal, the State conceded she had not. The misstatement that she had tested positive for the bacteria was an isolated statement among the 1800 plus pages of transcript. Based on these facts and all evidence presented, while the comment was improper it did not deprive the Petitioner of a fair trial.

Jones alleges that the prosecutor argued that Mr. Jones had confronted Susan Friend in an angry manner, without any support of such confrontation in evidence. (Petition, Doc. No. 15 at 32.) Respondent counters by stating that this claim is procedurally defaulted. Trial counsel failed to make a contemporaneous objection at the time of trial and did not bring the claim during direct appeal. (Return of Writ, Doc. No. 16 at 76.) The claim was brought in Jones's 26(B) motion, but Respondent argues he is unable to show cause to excuse his failure to bring the claim earlier. *Id.* at 69. Respondent argues that this claim is without merit as the State was commenting on the testimony as presented. *Id.* at 79. When on the stand, Friend stated that an alleged conversation between her and Jones had never taken place. (Trial Tr. Vol. XIX at 1798.) When she was later confronted by Jones regarding this she was a "little afraid." *Id.* The comment made in closing was a reasonable and logical argument based on the evidence presented. (Return of Writ, Doc. No. 16 at 79.)

***34** In reviewing this sub-claim the Court finds it to be procedurally defaulted as counsel failed to object at the proper time. Because ineffective assistance of appellate counsel can serve as "cause," the Court will consider the merits to the extent necessary to review the state courts' decision on the ineffective assistance claim. The claim is without merit as the State's argument in closing commented on Ms. Friend's testimony. The statement "[a]nd Miss Adams asked her, she was one of the people that Elwood Jones came up, and she was afraid of Elwood Jones, I think you remember her saying. And he confronted her in an angry fashion, remember I told you

that I hurt my hand setting up the dance floor? ..." is a logical argument. (Trial Tr. Vol. XIX at 1798.) Jones is not able to demonstrate prejudice from this statement, nor has he shown the state courts' decision on the ineffective assistance of appellate counsel claim was an objectively unreasonable application of clearly established federal law.

Next Jones contends that the comment arguing a link between bruise patterns on the victim and objects circumstantially connected with Mr. Jones, such as the walkie-talkie, shoes, and door chains, was not properly supported by any reliable or admissible evidence, and as such the comment itself was improper. (Petition, Doc. No. 15 at 32.) Respondent counters by stating that this claim is procedurally defaulted. Trial counsel failed to make a contemporaneous objection at the time of trial and did not bring the claim during direct appeal. (Return of Writ, Doc. No. 16 at 76.) The claim was concededly brought in Jones's 26(B) motion, but Respondent argues he is unable to show cause for his failure to bring the claim earlier. *Id.* at 69. Respondent additionally argues that this claim is without merit as the admissibility of evidence is left to the discretion of the trial court. *Id.* at 80. This Court agrees. As concluded above, the testimony was not constitutionally impermissible. In the absence of a contemporaneous objection, an assignment of error on direct appeal would likely have failed and therefore the state courts' determination that it was not ineffective assistance of appellate counsel to fail to make the claim is not objectively unreasonable.

Petitioner next alleges that the State improperly diminished the its burden of proof, placing the burden on the defense by arguing that the jurors had to deliberate upon the question of guilt or innocence. (Petition, Doc. No. 15 at 32.) Respondent counters by stating that this claim is procedurally defaulted. Trial counsel failed to make a contemporaneous objection at the time of trial and did not bring the claim during direct appeal. (Return of Writ, Doc. No. 16 at 76.) The claim was brought in Jones's 26(B) motion, but Respondent argues he is unable to show cause for his failure to bring the claim earlier. *Id.* at 69. Respondent additionally argues that this claim is without merit and that Petitioner's alleged error was taken out of context. *Id.* at 80. When considered in its entirety, the prosecutor was informing the jury of its role in the culpability phase as opposed to the mitigation phase. *Id.*

***35** This claim is procedurally defaulted. In the alternative it is without merit. The comment made by the prosecution in closing was; "[a]nd in mentioning sentencing, I would indicate to you that Judge Winkler will also tell you that sentencing shouldn't even be in your mind at this stage of the trial. At this point you are to decide guilt or innocence." (Trial Tr. Vol. XIX at 1734.) This comment did not diminish or shift the burden of proof. During jury instructions the trial judge properly instructed the jury as to burden of proof. (Trial Tr. Vol. XIX at 1833.)

Next Petitioner asserts the State improperly argued, without evidence in the record, that the banquet department of the Embassy Suites was the only department which used the walkie-talkies capable of making the marks on the victim's body. (Petition, Doc. No. 15 at 32.) Respondent concedes that this claim was properly raised in direct appeal and as such may be considered on the merits. (Return of Writ, Doc. No. 16 at 73.) It is further argued that this claim is without merit as Petitioner cannot demonstrate that the statement was so egregious that it rendered his trial fundamentally unfair. *Id.* The Ohio Supreme Court held that the statement was harmless even though there was other evidence that different departments had similar radios. *State v. Jones,* 90 Ohio St.3d 403, 420–421, 739 N.E.2d 300, 318–319 (2000).

This Court concludes the state courts' conclusion was neither contrary to nor and unreasonable application of clearly established federal law. The comment was isolated rather than extensive and there is no evidence that such comment intentionally inaccurate. Additionally, defense counsel objected immediately to the statement and the State rephrased to admit that other departments, aside from banquet, may have used similar walkie talkies. (Trial Tr. Vol. XIX at 1812–13.) In view of other testimony presented from witnesses that other department used similar walkietalkies, defense counsel's arguing the State's hole in this assertion during their own closing argument, and the trial court's instruction that closing arguments are not to be considered evidence, it does not appear that such a comment would mislead the jury. (Trial Tr. Vol. XIV at 1074–1075, 1109); (Trial Tr. Vol. XVI at 1488–1489); (Trial Tr. Vol. XIX at 1723, 1772–1773, 1827.) This statement was not likely to have a bearing on the outcome of the trial in light of the other evidence presented. *Angel v. Overberg,* 682 F.2d 605, 608 (6th Cir.1982).

Next Petitioner challenges the statements made by the Prosecution regarding Mr Jones's alleged girlfriend, Earlene Metcalfe.[6] (Petition, Doc. No. 15 at 32.), specifically that the State alleged Metcalfe had lied for Jones. *Id.* Defense counsel objected and that objection was sustained. *Id.* The State however, continued to characterize Metcalfe as a liar and went on to discuss the shoes taken from her home. *Id.;* (Trial Tr. Vol. XIX at 1799); (Trial Tr. Vol. XIX at 1800.) Respondent does not allege procedural default for this sub-claim, but rather argues that it is without merit. (Return of Writ, Doc. No. 16 at 74.) In considering these statements, which both state courts held to be "improper because they alluded to facts not in evidence," Respondent argues the Court must consider the totality of the circumstances. *Id.; State v. Jones,* 90 Ohio St.3d at 420–421, 739 N.E.2d 300; *State v. Jones,* 1998 Ohio App. LEXIS 3938 (1st Dist.1998). When considered under the totality of the circumstances, respondent asserts, the comments were not outcome-determinative, and Jones fails to show that he did not receive a fair trial. (Return of Writ, Doc. No. 16 at 74.)

6 Variations of spelling for Earlene Metcalfe's name appear throughout the record. For the purpose of this Report and Recommendation, the Court adopts the spelling used by the Ohio Supreme Court.

***36** The portion of testimony in dispute is reproduced below:

> .... well, maybe he thinks he told her and he didn't. But we know that Erlene Metcalff lied. You know who is Erlene Metcalff. She is Butch Jones' girlfriend. (Objection and trial court sustains the objection)
>
> * * * *
>
> She told Randy Hughes, who is the kitchen manager I think, that she witnessed Elwood Jones cut his hand. She told him that and that's on the form and you'll have that. We know that that's a lie, because he said there were no witnesses to this alleged cutting of his hand. She lied for him.
>
> Why would she do that? What do we know about her? We know that she's his girlfriend. We know that his shoes were found under her bed in the master bedroom..... Yvonne Kinard, Butch Jones' wife, is probably a very nice person. And she is a person who's been taken advantage of by the defendant. He's got a wife that stayed with him, stayed by his side, would even come to court and testify for him. At the same time, he's got another relationship that he spends a lot of time with, this other woman.
>
> Now she didn't know that he kept personal belongings at her house. Now, Brenda Wallace told you, and she is the executive housekeeper, that Elwood Jones wore dress shoes to work. You'll have a pair of dress shoes that she took out of the defendant's—excuse me—Erlene Metcalff's house from under her bed. It's the same shoes that Mike Trimpe told you that are consistent with making the marks on her chest.
>
> Miss Adams told you that how do we know they are the defendant's shoes? How do we know they are the same size? Don't you think if they wouldn't have been his shoes or his size that someone would have come up here and told you he wears this size. There are this size. They are obviously not his. This wasn't done, was it? Just an argument to you to search for doubt. Doubt that's not there.

(Trial Tr. Vol. XIX at 1799–1801.) These remarks were more extensive and deliberate than the previous instances of alleged misconduct and did allude to facts not in evidence. These comments are improper. However, when viewed against the other evidence presented and in the totality of the circumstances, though improper, the comments did not deprive Petitioner of a fair trial. Testimony was presented as to ownership of the shoes. The Court also notes that a portion of Petitioner's argument—misconduct arising from the statement regarding the shoes—could be considered rebuttal to the defense's closing. During closing defense counsel argued that the shoes did not belong to Jones, as there was no discussion or evidence presented as to the size of the shoes or the shoe size worn by Jones, his wife was not able to identify the shoes and she stated in her testimony that Jones wore black shoes, not brown.[7] (Trial Tr. Vol. XIX at 1771.)

7 "Let's talk about the shoes. In the stipulation those are referred to as taken from Elwood Jones. Well, you heard the testimony. They were taken from the house on Park Avenue.

Do we know for sure that they were his? What evidence could have been presented to you on that? There's no size. We don't know what size shoe he wears. We don't know if there were other males in the household.

> We do know this, Yvonne said she has never seen them before. Of course they were not found at her house. She also said that when he went to work he wore black shoes because that was his uniform. He work [sic] black pants, a gray shirt and black shoes. Not brown ones. They wouldn't go with his uniform. And you heard he always dressed well. He wore black shoes." (Trial Tr. Vol. XIX at 1771.)

Next Jones alleges that the State denigrated the role of defense counsel, suggesting that they were attempting to hide the truth and unfairly accuse others of the crime, even though defense counsel was doing no more than suggesting that other employees had an opportunity to commit the crime. (Petition, Doc. No. 15 at 33.) Additionally, the State alluded to improper collusion between defense counsel and their expert. *Id.*

***37** Respondent does not allege procedural default, but rather argues that this claim is without merit. (Return of Writ, Doc. No. 16 at 74–75.) Respondent asserts that the State was questioning points of defense counsel's opening statement and the reliability of the expert witness's opinion. *Id.* at 75. The state court held that the statements were "fair argument for closing," and that "given the substantial evidence submitted in this case, ... these isolated comments ... were not prejudicial." (Return of Writ, Doc. No. 16 at 75); *State v. Jones,* 1998 Ohio App. LEXIS 3938 *29 (1st Dist.2000); *State v. Jones,* 90 Ohio St.3d 403, 421, 739 N.E.2d 300, 318 (2000).

The comments made by the State regarding other suspects appears to be a fair rebuttal to defense closing arguments that "the problem was they had never looked at anybody who didn't have a record as to whether that person could be a suspect or not."[8] (Trial Tr. Vol. XIX at 1756.) Likewise, the trial court ruled that comment about defense counsel and their expert witness was a actually comment on defense's opening statement and counsel is entitled to comment on what opposing counsel said during the opening. (Trial Tr. Vol. XIX at 1802.) This Court agrees. Neither comment were improper nor did they mislead the jury nor deprive the Petitioner of a fair trial. The decision of the state court was neither contrary to nor an unreasonable application of federal law.

8 "That's why we brought up Bill McCall, not because we think Bill McCall did this, but because he should have been looked at. There were things about his behavior that should have been examined in an investigation such as this of such a major crime. But he wasn't." (Trial Tr. Vol. XIX at 1756.)

> "Who stands out? Greg Henry. Remember Greg Henry? He was one of the last people to testify. He works in maintenance. He gets in between 6:30 and 7 in the morning. He has access to keys, key making machines and radios.
>
> You heard Charles O'Banion testify that in the maintenance department some of the radios have casings such as the one that is on the one in evidence. It's not unusual to see maintenance in any part of the hotel, that's what Randy Hughes told you ....
>
> And maybe they don't, because maybe it was Greg's radio that made that mark on her body. Maybe he didn't do it. But he sure should have been checked out, because he told you that he told the police the same story that he sat here and said to you. We don't know where Greg Henry was between time he got to work and the time that this happened, and his story sure doesn't make any sense." (Trial Tr. Vol. XIX at 1784–1787.)

Finally, Petitioner alleges that the Prosecution relied on testimony about the pendant which it knew to be incorrect. (Traverse, Doc. No. 144 at 62.) Specifically, the comment, "What about the pendant? What was said to you about the pendant? Nothing. You know why? Because they can't explain the pendant. They can't explain it at all." *Id.;* (Trial Tr. Vol. XIX at 1813.) This sub-claim was not raised in the Petition. (Doc. No. 15); (Doc. No. 82 at 9.) Because it was first presented in the Traverse rather than in the habeas petition, it is not properly before this Court which declines to address it. *Tyler v. Mitchell,* 416 F.3d 500, 504 (6th Cir.2005); *United States v. Barrett,* 178 F.3d 34, 46 (1st Cir.1999); *Jackson v. Duckworth,* 112 F.3d 878, 880 (7th Cir.1997). Additionally, this sub-claim is procedurally defaulted as it was based on the record, should have been objected to at the time of trial, and should have been raised as a claim on direct appeal.

Next Jones claims that the Prosecutor improperly attacked credibility of defense witness Jimmy Johnson by eliciting evidence of his criminal history through a police officer. (Petition, Doc. No. 15 at 26.) Respondent replies that neither the prosecution nor the witness stated that Johnson had a criminal history. (Return of Writ, Doc. No. 16 at 81.) The exchange between the witness, who was a police officer, and the prosecutor, did however imply that there was a criminal history. (Trial Tr. Vol. XVII at 1606.) On cross-examination the officer was asked if Jimmy Johnson is "very well known to your department."

Id. The Court does note that there was no elaboration on how Johnson was known to the police department or what was meant by "well-known." Because it was not elaborated on, any error resulting from this testimony was not egregious enough to render the trial fundamentally unfair or deny Jones his rights. In light of the strength of the evidence against Jones, this statement was not likely to have had a bearing on the outcome of the trial. *Angel v. Overberg,* 682 F.2d 605, 608 (6th Cir.1982).

***38** Petitioner asserts that the prosecution made similar misstatements in their closing during the mitigation phase. (Petition, Doc. No. 15 at 34.) Specifically the State was trying to mislead the jurors regarding the legal standards applicable to their deliberations.

> But one thing both sides stressed when we started this case, when you get to this part of the case can you set aside your personal feelings and follow the law as the judge gives it to you? I'm not just the one asking that; they asked you that also. Now all of a sudden you are given different instructions from the defense and I'm not going to. I'm going back to what we asked you right off the bat, what Judge Winkler tells you to do. If you do that, we will be satisfied.

(Petition, Doc. No. 15 at 34);(Trial Tr. Vol. XXII at 1942.) The State continued by arguing that defense could have presented mitigation from family members or doctors if they had wished. (Petition, Doc. No. 15 at 34); (Trial Tr. Vol. XXII at 1946–1947.) Defense counsel repeatedly objected to these comments. The objections were overruled. (Petition, Doc. No. 15 at 34); (Trial Tr. Vol. XXII at 1946–1947.) The Court holds that the jurors were properly instructed by the trial judge on the legal standards.

Additionally, Petitioner alleges prosecutorial misconduct from the portion of the State's closing in which they state that the jurors could and should consider the nature and circumstances of the crimes:

> What is worth more to him at that point, the life of this lady who has absolutely done nothing to him or a trinket? He could have left her alive. What's his choice? Right here. (Indicating.) ... That's the value he put on that lady's life. I trust when you weigh that aggravating circumstance you will give Miss Nathan's life more worth than he did.

(Petition, Doc. No. 15 at 34); (Trial Tr. Vol. XXII at 1951.) Defense counsel objected to this line of argument. (Trial Tr. Vol. XXII at 1951.) The objections were overruled, thus permitting the jurors to consider the nature and circumstances of the offense, and the loss of life, as aggravating circumstances, contrary to Ohio Rev.Code § 2929.04. (Petition, Doc. No. 15 at 35.) Jones argues that "by violating Ohio's clear procedures for weighing aggravating circumstances against mitigating factors when deliberating upon the appropriateness of selecting death for Mr. Jones, the prosecutors and the trial court transgressed federal constitutional barriers which require states to articulate rational, non-arbitrary guidelines for capital jurors." (Petition, Doc. No. 15 at 35.)

The trial court properly instructed the jury on what could be considered in their weighing process. (Trial Tr. Vol. XXII at 1956–1957.) A jury is presumed to follow the instructions of the court. This sub-claim is without merit.

Third Ground for Relief

The fairness of Mr. Jones's trial and the reliability of his convictions and death sentence were undermined by the absence of exculpatory and impeachment evidence that the prosecution should have disclosed. In the alternative, defense counsel were ineffective for failing to discover the exculpatory and impeachment evidence.

***39** A. Evidence of Serious Irregularities with the Blue Ash Police Department's Evidence Records

B. Evidence of Criminal Acts and Suspicious Employees at the Embassy Suites Hotel

C. Other Undisclosed Materials Cast Further Doubt on the Reliability of the Outcome of Mr. Jones' Trial and Suggest that Additional Undisclosed Information May Still Exist.

(Petition, Doc. No. 15 at 37); (Traverse, Doc. No. 144 at 70.)

Respondent concedes that the portions of this claim relating to the property tags and police reports about crime were presented in post-conviction proceedings. (Return of Writ, Doc. No. 16 at 84, 138.) The Court of Appeals addressed these portions on the merits and determined that none of the evidence was *Brady* material. *Id.* at 84. See also *State v. Jones,* 2000 Ohio App. LEXIS 6197, *11–14 (Ohio App. 1st Dist. Dec. 29, 2000). Respondent asserts the sub-claims addressing the pendant, coroner's opinion as to the bruise patterns, and the documents showing the victim had hepatitis were not raised in the state courts. *Id.* Respondent argues that the claims are unexhausted but without merit, so it is proper for this Court to deny them.

The State has a duty to produce exculpatory evidence in a criminal case. If the State withholds evidence and it is material, the conviction must be reversed. *Brady v. Maryland,* 373 U.S. 83, 83 S.Ct. 1194, 10 L.Ed.2d 215 (1963). "Evidence is material only if there is a reasonable probability that, had the evidence been disclosed to the defense, the result of the proceeding would have been different. A 'reasonable probability' is a probability sufficient to undermine confidence in the outcome." *United States v. Bagley,* 473 U.S. 667, 683, 105 S.Ct. 3375, 87 L.Ed.2d 481 (1985).

There are three essential components of a true *Brady* violation: the evidence at issue must be favorable to the accused, either because it is exculpatory, or because it is impeaching; that evidence must have been suppressed by the State, either willfully or inadvertently; and prejudice must have ensued. *Strickler v. Greene,* 527 U.S. 263, 119 S.Ct. 1936, 144 L.Ed.2d 286 (1999):

> In *Brady,* this Court held "that the suppression by the prosecution of evidence favorable to an accused upon request violates due process where the evidence is material either to guilt or to punishment, irrespective of the good faith or bad faith of the prosecution." 373 U.S., at 87, 83 S.Ct. 1194, 10 L.Ed.2d 215. We have since held that the duty to disclose such evidence is applicable even though there has been no request by the accused, *United States v. Agurs,* 427 U.S. 97, 107, 96 S.Ct. 2392, 49 L.Ed.2d 342 (1976), and that the duty encompasses impeachment evidence as well as exculpatory evidence, *United States v. Bagley,* 473 U.S. 667, 676, 105 S.Ct. 3375, 87 L.Ed.2d 481 (1985). Such evidence is material "if there is a reasonable probability that, had the evidence been disclosed to the defense, the result of the proceeding would have been different." *Id.,* at 682, 473 U.S. 667, 105 S.Ct. 3375, 87 L.Ed.2d 481; see also *Kyles v. Whitley,* 514 U.S. 419, 433–434, 115 S.Ct. 1555, 131 L.Ed.2d 490 (1995). Moreover, the rule encompasses evidence "known only to police investigators and not to the prosecutor." *Id.,* at 438, 514 U.S. 419, 115 S.Ct. 1555, 131 L.Ed.2d 490. In order to comply with Brady, therefore, "the individual prosecutor has a duty to learn of any favorable evidence known to the others acting on the government's behalf in this case, including the police." *Kyles,* 514 U.S., at 437, 115 S.Ct. 1555, 131 L.Ed.2d 490.
>
> ***40** These cases, together with earlier cases condemning the knowing use of perjured testimony, illustrate the special role played by the American prosecutor in the search for truth in criminal trials. Within the federal system, for example, we have said that the United States Attorney is "the representative not of an ordinary party to a controversy, but of a sovereignty whose obligation to govern impartially is as compelling as its obligation to govern at all; and whose interest, therefore, in a criminal prosecution is not that it shall win a case, but that justice shall be done." *Berger v. United States,* 295 U.S. 78, 88, 55 S.Ct. 629, 79 L.Ed. 1314 (1935).

Strickler, 527 U.S. 280–81. *Accord, Jamison v. Collins,* 291 F.3d 380 (6th Cir.2002).

Brady did not create a general constitutional right to discovery in criminal case; rather, the rule established therein "is concerned only with cases in which the government possesses information which the defendant does not, and the government's failure to disclose the information deprives the defendant of a fair trial." *United States v. Mullins,* 22 F.3d 1365, 1371 (6th Cir.1994). No Brady violation exists where the defendant knew, or should have known, the essential facts permitting him to take advantage of any exculpatory information.' " *United States v. Clark,* 928 F.2d 733, 738 (6th Cir.), *cert. denied,* 502 U.S. 846, 112 S.Ct. 144, 116 L.Ed.2d 110 (1991); *United States v. Grossman,* 843 F.2d 78, 85 (2nd Cir.1988), *cert. denied,* 488 U.S. 1040, 109 S.Ct. 864, 102 L.Ed.2d 988 (1989)); *Coe v. Bell,* 161 F.3d 320, 344 (6th Cir.1998) (There is no *Brady* violation where information is available to the defense "because in such cases there is really nothing for the government to disclose.") *Bell v. Bell,* 512 F.3d 223 (6th Cir.2008) (en banc) (*Matthews*

applied even when the prosecutor denied the existence of some of the material.)

A. Evidence of Serious Irregularities with the Blue Ash Police Department's Evidence Records

In addressing this, and Petitioner's next sub-claim, the State court held that:

> In his eighth claim for relief, Jones argues that his convictions should be vacated because the prosecutor concealed exculpatory evidence. In a similar vein, in his thirtieth and thirty-fifth claims, he argues that his trial counsel were rendered ineffective because the prosecutor withheld exculpatory evidence. (We believe the fundament of these last two claims concerns whether the prosecutor withheld exculpatory evidence and review the claims as such.)
>
> In the eighth and thirteenth claims, Jones argues that the prosecutor withheld Blue Ash Police Department property tags that contained evidence of irregularities that were favorable to him. For example, there were gaps in the sequentially numbered tags where multiple items were collected on a given date; the tag relating to a purse appeared to be wrongly dated; some of the dates on the tags appeared to have been altered; one of the tags stated "Photo evidence-negative results from FBI shoe print exam"; there were no tags for Jones's car keys; a properly tag referred to a bloody handkerchief taken from Jones, but there was no evidence of forensic tests having been done on the handkerchief; and although the tag for the handkerchief was dated September 12, 1994, the tag number corresponded sequentially to items taken from Jones's car on September 14, and not to items taken from him on September 12.
>
> ***41** In his thirty-fifth claim, Jones's contends that the prosecutor failed to disclose copies of the Blue Ash Police Department's yearly reports of criminal activity from the department's hotel/motel interdiction unit. According to Jones, the evidence could have further advanced Jones's claim of innocence by demonstrating the following: (1) that the Embassy Suites Hotel routinely hired criminals; (2) that the hotel's guests were routinely crime victims; (3) that the hotel rooms were routinely used by "unsavory characters," and (4) that several thefts had occurred at the hotel after Jones was no longer present, including an incident in which someone tried to enter a guest's room with a key.
>
> In support of the first two claims, Jones provided to the court below copies of the property tags, an affidavit of S. Adele Shank, an attorney experienced in representing capital defendants, and the affidavit of Catherine Adams, one of Jones's trial counsel. Adam's affidavit stated that neither trial counsel had reviewed the property tags. In support of his thirty-fifth claim, Jones presented the 1994 yearly report. The trial court ignored Jones's claim that the state had withheld exculpatory material in violation of *Brady v. Maryland,* and erroneously concluded that Jones's eighth and thirtieth claims concerned chain-of-custody issues that were barred by *res judicata.* It found that his thirty-fifth claim merely second-guessed trial counsel's strategy.
>
> The suppression by the state of evidence favorable to a defendant is a violation of the defendant's due-process rights if the evidence is material to guilt. The withheld evidence may be exculpatory or impeaching, but it must be "material" to be the subject of a *Brady* violation. To be material to guilt, the withheld evidence must be such that there is a reasonable probability that had it been disclosed, the result of the proceeding would have been different. To determine the materiality of evidence, "[t]he question is not whether a defendant would more likely than not have received a different verdict with the evidence, but whether in its absence, he received a fair trial, understood as a trial resulting in a verdict worthy of confidence." Thus, a "reasonable probability" of a different result exists where the state's suppression of evidence "undermines confidence in the outcome of the trial." As this court has explained, "This standard of materiality applies regardless of whether the evidence is specifically, generally, or not at all requested by the defense."
>
> To prevail on the alleged *Brady* violation, Jones had to demonstrate that the prosecutor withheld material evidence favorable to him. While the properly tags were of marginal impeachment value, we cannot conclude that the withholding of them undermined the confidence of Jones's trial. We also conclude that the 1994 hotel/motel interdiction unit's report was neither exculpatory nor material. Thus, the evidence Jones proffered either was not cogent or failed to demonstrate substantive grounds for relief.

*42 *State v. Jones, State v. Jones,* 2000 Ohio App. LEXIS 6197, *11–14 (Ohio App. 1st Dist. Dec. 29, 2000).

Jones argues that if the jurors knew of the irregularities in the numbering of the property tags, it would have seriously undermined the credibility and reliability of the State's evidence regarding the pendant. (Petition, Doc. No. 15 at 37.) He argues that these irregularities cast doubt on the integrity of the State's case and are favorable to the defense and as such should have been disclosed to him as *Brady. Id.* In regard to the tags, Petitioner states that they are self-triplicating, five by seven inch preprinted cards bearing the name and address of the Blue Ash Police Department. *Id.* at 38. Each property tag has a pre-printed sequential number appearing in the upper left-hand corner. *Id.* There are places for recording information such as date and time the evidence was taken, description of the evidence, from whom and where it was taken, and other general information. *Id.* Multiple items collected on a given date would be recorded on a series of sequentially numbered property tags. *Id.* at 39. Therefore, any gaps in the sequentially numbered property tag or any handwritten date which falls outside the sequence of other items collected around the same time is suspicious and irregular and should have been revealed to the defense. *Id.* In support of his claim, Jones cites to property tags relating to Elaine Schub's purse, property tags pertaining to the search of his car, a property tag for a photograph submitted to the FBI, the absence of a property tag for Jones's car keys, and a property tag for a bloody handkerchief. *Id.* at 39–41. He argues that these property tags are not in proper order, appear to have the date altered, or the evidence collected was not used at trial. He says this clearly shows mishandling and potential misconduct and could have been used to impeach testimony at trial, specifically that of Officer Bray who found the pendant in the Jones's car. *Id.* at 41.

Respondent counters by arguing that the property tags were not exculpatory or material. (Return of Writ, Doc. No. 16 at 87.) The information contained on the property tags fails to meet the *Brady* standard and does not advance Jones's theory that the Blue Ash Police Department planted evidence. *Id.* The car keys were not entered on a property tag but rather were secured by a police officer in his desk. This is consistent with the testimony given at trial. (Trial Tr. Vol. XV at 1207.) The property tag pertaining to the FBI shoeprint exam is not exculpatory as the State did not rely on shoeprint evidence to establish Jones's identity; to the contrary an expert testified that the bruise on the victim's chest was consistent with having been made by the shoe, however, was not sufficiently unique enough to determine if the bruise was made by these shoes to the exclusion of all other shoes. *Id.* at 89; (Trial Tr. Vol. XIII at 896.) Likewise the bloody handkerchief did not play any part in establishing guilt or innocence. (Return of Writ, Doc. No. 16 at 89.) Respondent notes that the investigation lasted over a year, during which time evidence was collected and tracked, which may account for some of the "glaring anomalies." *Id.* Finally, Respondent states that property tag 28376 clearly establishes that Nathan's pendant was recovered in the trunk of Jones's car, therefore the property tags do not exculpate Jones but rather implicate him as the perpetrator. *Id.*

*43 The property tags were not enough to implicate a *Brady* violation. While they may have provided marginal impeachment evidence, in order to be considered *Brady* there must be a reasonable probability that the outcome of the trial would have been different. *Strickler v. Greene,* 527 U.S. 263, 119 S.Ct. 1936, 144 L.Ed.2d 286 (1999). This is not the case. Jones speculates as to police misconduct and planting of evidence, but this speculation does not amount to prejudice or a reasonable probability that, had the property tags been disclosed to the defense, the result of the proceeding would have been different The decision of the state court that the property tags were not *Brady* material was neither contrary to nor an unreasonable application of federal law.

B. Evidence of Criminal Acts and Suspicious Employees at the Embassy Suites Hotel

Next Jones alleges that the State failed to disclose copies of the Blue Ash Police Department's yearly reports of criminal activity, and the fact that other Embassy Suites employees had criminal records. (Petition, Doc. No. 15 at 42); (Traverse, Doc. No. 144 at 80.) He states that had this information been disclosed, then defense's theory could have been further advanced by "the presentation of evidence that Embassy Suites Hotel routinely hired many employees with criminal records; that Embassy Suites Hotel guests were routinely victims of crimes; and that Embassy Suites Hotel rooms were routinely utilized by unsavory characters involved in drugs and prostitution." (Petition, Doc. No. 15 at 42.)

Jones points out that contained within this Interdiction Unit report is the fact that Embassy Suites had the most police runs and criminal arrests in 1994 and 1995. (Traverse, Doc. No. 144 at 82.) Additionally, the hotel routinely hired people with criminal records, and many of these employees had access to the master key. *Id.* Specifically, Jones cites to a report dated December 27, 1994, months after Nathan's murder, that recorded a guest's report of an incident of someone attempting to gain access to their hotel room, which police later determined was an employee with an unauthorized key. (Petition, Doc. No. 15 at 43.) Jones also points to other reported thefts on September 4, 6, 7, 15 and October 9, 10, 12, 20, 1994. *Id.* He claims that the reports of theft after he was no longer employed support his claim of innocence. *Id.*

Petitioner's counsel expounded on this during the evidentiary hearing before this Court. They contended that the above information was *Brady* evidence and that it, as well as access to questionnaires filled out by guests of the hotel on the morning of the murder, would have been beneficial in their defense. (Evid. Trial Tr. 9/25/07 at 99–103, 113–118, 215–217, 220–222, 226–241, 251–253.) If the reports and questionnaires had been made available then, trial counsel could have followed up on the information contained therein, including reports of suspicious activity and suspicious people in the hotel. (Evid. Trial Tr. 9/25/07 at 99–102, 108–109, 111, 113–119, 215–218, 224–241, 245–255.) Additionally Jones cites to the compilation put together by the Blue Ash Police Department detailing hotel employees' locations at various times on the morning of the murder, whether alibis could be verified, their past criminal history, and whether they had been subjected to a polygraph exam.

***44** Respondent counters by stating that the claim is without merit as Jones fails to present evidence sufficient to show that the documents were *Brady* and that they would have been material to the outcome of his trial. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 16.)

Jones bases his argument that this was exculpatory evidence on "subjective" comments made by hotel guests, such as: people that seemed "out of place" at the Embassy; confusion by housekeeping as to whether or not a room had already been cleaned; a desire for better security measures which included all hotel employees identifying themselves prior to entering a room to do maintenance; and comments reflecting the state of the hotel's construction project. (Respondent's Reply to Traverse, Doc. No. 82 at 12–13.) Even taken together these comments do not point to "other criminal activity that night" or "a gang operating in the hotel" as alleged by Petitioner. *Id.;* (Traverse, Doc. No. 144 at 90.)

The State further asserts that Petitioner is essentially arguing that the State should have disclosed every run-of-the-mill crime that occurred at this hotel regardless of whether or not it had any connection to this case. (Return of Writ, Doc. No. 16 at 90.) Citing the December 27th event, Respondent argues it was not material to Jones's trial as the State did not assert that Jones had the only master key to the hotel. Rather the evidence showed that Jones had a master key that he signed out on the morning of the murder, that the key was not signed back in, and that a key to the hotel was later found in Jones's car. (Return of Writ, Doc. No. 16 at 91.) Likewise, the other crimes listed in the 1994 Interdiction Report are not exculpatory as there is no correlation between Nathan's murder and the thefts, drug use, prostitution, and other such acts that were reported for that year. *Id.* Nothing in this report implicates someone else as the murderer nor exonerates Jones. *Id.*

Respondent counters the *Brady* claim as to the police compilation by noting that the report was generated as a summary from the employee interviews conducted at hotel. (Respondent's Reply to Traverse, Doc. No. 82 at 15.) Defense counsel was permitted to attend this meeting at the hotel, to talk to anyone they wanted, to look at hotel records, and to generate their own summary report. *Id.; see also* (Piepmeir Deposition at 49); (Adams Deposition at 69–70.) As for Jones's attempt to cast suspicion on other employees at the hotel who had a conviction in their past, or similar opportunity to commit crimes, it is not even known if these people were at the hotel the morning of the murder and as such cannot be considered material nor exculpatory. (Return of Writ, Doc. No. 16 at 91.) Respondent further notes that a past criminal record alone is not enough to be material as Jones was the employee found with the pendant in the trunk of his car. *Id.*

This claim is without merit. The Interdiction report showed that there were other crimes committed at this hotel during the 1994 calendar year, but it does not connect any of these crimes with what occurred on September 3, 1994, nor does it undermine the confidence

in the trial's outcome. The evidence at trial showed that Jones had access to a master key, that it was signed out the morning of the murder and was not signed back in. (Trial Tr. Vol. XVI at 1442–1443 .) The evidence further proved that a hotel key was later discovered in the in the trunk of Jones's car, along with the pendant, and that this key did in fact open the door to room 237. (Trial Tr. Vol. XV at 1216, 1219, 1329.) Furthermore, at some point around the day of the murder, Mr. Jones suffered a wound to his hand and developed an infection which results from a bacteria often transferred in "fight bite" type wounds. (Trial Tr. Vol. XIV at 990–991, 994, 1001, 1005); (Trial Tr. Vol. XV at 1334, 1336.)

***45** The compilation summary of Embassy employee interviews created by the Blue Ash Police Department is also not *Brady* material as "the defendant knew or should of known of information, or where information is made available to him through another source." *United States v. Mullins,* 22 F.3d 1365, 1371 *citing United States v. Clark,* 928 F.2d 733, 738 (6th Cir.1991) and *United States v. Grossman,* 843 F.2d 78, 85 (2nd Cir.1988). Defense counsel had opportunity to interview these people and did interview many of them. (Evid. Trial Tr. 9/25/07 at 221.) Jones has not shown that the State withheld evidence, nor has he shown that there was a reasonable probability that the above contested evidence been disclosed, the result of the proceeding would have been different. The decision of the state court of appeals was neither contrary to nor an unreasonable application of federal law.

C. Other Undisclosed Materials Cast Further Doubt on the Reliability of the Outcome of Mr. Jones' Trial and Suggest that Additional Undisclosed Information May Still Exist.

In his next sub-claim Petitioner alleges that other undisclosed material, including the descriptions of the pendant, reports of potential witnesses, reports of other activities at the hotel, and the coroner's report showing that Nathan tested positive for hepatitis should have been considered *Brady* material and given to the defense. As a result of this failure, the reliability of his verdict is challenged. (Traverse, Doc. No. 144 at 83–93); (Motion to Amend Petition, Doc. No. 142.)

Respondent counters by arguing that this portion of the claim was never raised in state court. (Return of Writ, Doc. No. 16 at 92); (Respondent's Post–Evidentiary Hearing Brief, Doc. No. 147 at 4–5.) Petitioner argues that he can establish cause and prejudice as the items in question were not turned over to defense during the state-court proceedings, and only discovered during habeas proceedings. (Traverse, Doc. No. 144 at 83.) Therefore, Petitioner asserts that he has shown cause for failing to raise at an earlier time and that because this claim has not been presented in the state courts, the Court has no state decision to defer to and the pre-AEDPA *de novo* standard applies. *Id.*

Respondent also argues that this claim was not properly presented in the Petition and even if Petitioner were to amend it at this point in time, the new amended claim would be barred under the one-year statute of limitations. (Respondent's Post–Evidentiary Hearing Brief, Doc. No. 147 at 5.) Petitioner filed a Motion to Amend Petition to add these sub-claims on November 13, 2007. (Doc. No. 142.) Respondent filed her Opposition to Motion to Amend Petition on November 14, 2007, to which Petitioner replied on December 4, 2007. (Doc. No. 145); (Doc. No. 146.) The Court issued a Decision and Order granting the Motion to Amend the Petition on December 10, 2007. (Doc. No. 148.) The Court held that the amendment to this ground for relief is not barred by the statute of limitations as interpreted in *Mayle v. Felix,* 545 U.S. 644, 125 S.Ct. 2562, 162 L.Ed.2d 582 (2005), because it does not "assert a new ground for relief supported by facts that differ in both time and type from those set forth in the original pleading."

***46** Respondent also notes that these sub-claims are not exhausted and that there are state corrective processes available for Jones to exhaust this claim, in the form of a successive post-conviction petition or motion for a new trial based upon newly discovered evidence which could not have been discovered in time for the first petition. (Response in Opposition to Motion to Amend, Doc. No. 145.) Respondent further correctly notes that this Court may not grant a petition based on an unexhausted claim, but is permitted to deny a petition based on an unexhausted claim which lacks merit. *Id.;* 28 U.S.C. § 2245(b)(1)(A); 28 U.S.C. § 2245(b)(2). Petitioner does not respond to the exhaustion argument but instead argues that the claim is not procedurally defaulted. This Court, when permitting the amendments to the Petition, stated that "if it finds the claims to be potentially meritorious, the question of a stay to allow their submission to the state courts will be addressed at that time."

The evidentiary hearing held before this Court on September 24–25, 2007, addressed the below sub-claims. During the hearing Petitioner presented testimony from both his trial attorneys and from defense expert witness, Dr. Solomkin.

1. The Pendant

In his first sub-claim Jones argues that the various inconsistent descriptions of the pendant, as well as the inconsistencies in the origin of the pendant and whether it had been custom crafted, should have been disclosed to him. (Traverse, Doc. No. 144 at 84.) Specifically, Jones argues that the withheld items included: 1) the interview of Val Nathan, son of the victim, during which he described the necklace differently from the pendant recovered; 2) the phone interview of Ira Nathan, brother-in-law of the victim, who indicated that the necklace was not custom crafted from an engagement ring; and 3) the interview of Rhoda Nathan's friend Eileen Schub who described the necklace differently from the one she identified at trial. (Traverse, Doc. No. 144 at 84.)

In support of his claim Jones states that the initial search warrant affidavit shows that the officers were looking for a necklace with a pendant comprised of seven rows of tubular metal, silver in color, containing three diamonds. (Traverse, Doc. No. 144 at 84.) Val Nathan, during an interview, told officers that he remembered the pendant as being three staggered bars, with three diamonds, and silver in color. (Traverse, Doc. No. 144 at 85.) When shown the recovered pendant Nathan was fairly certain that the pendant was not the same pendant as worn by his mother "at all times," though after viewing family photographs of the victim wearing her pendant, he was sure it was in fact the same. *Id.* Ms. Schub described the necklace as being an odd shape, a criss-cross having a few diamonds. (Traverse, Doc. No. 144 at 87.) Jones alleges that the withheld descriptions should be considered *Brady* evidence and that they would have been material in his case as defense counsel would have structured its cross-examination differently, or they would have potentially subpoenaed family members to be witnesses for the defense. (Traverse, Doc. No. 144 at 86); (Evid. Trial Tr. 9/25/07 at 94, 210, 214, 283, 106, 209, 214, 280–284, 290.)

***47** Additionally, Ira Nathan claimed that the pendant was not custom made as originally believed but was purchased at Michael's Jewelry Store in the Bronx. *Id.* The owner of the store remembered the victim's husband, but did not recall a transaction involving the pendant. *Id.* Other notes suggest that it was purchased from a store in Pellam Bay. (Traverse, Doc. No. 144 at 85); (Evid. Trial Tr. 9/25/07 at 106, 213.) Defense counsel argues that had they known this information back at the time of trial they would have investigated if the pendant was one of a kind or mass produced and potentially argued this to the jury. (Traverse, Doc. No. 144 at 86); (Evid. Trial Tr. 9/25/07 at 88, 90–91, 106, 167, 169, 176, 209.) Jones concludes this argument by alleging that the State used this *Brady* material to taunt the defense in closing, asking jurors, "What about the pendant? What was said to you about the pendant? Nothing. You know why? Because they can't explain the pendant. They can't explain it at all." (Traverse, Doc. No. 144 at 84.)

Respondent counters by stating that defense counsel was aware of the discrepancies in the description of the pendant as it was made available through the affidavit for the search warrant and the return of the search warrant, as well as the actual pendant itself. (Reply Brief to Traverse, Doc. No. 82 at 11); (Evid. Trial Tr. 9/25/07 at 83, 190, 194.) Respondent is also argues that Val Nathan changed his mind as to his original description of the pendant after seeing a photo of his mother wearing the pendant. These photos were admitted at trial and given to defense counsel in advance. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 6); (Evid. Trial Tr. 9/25/07 at 84, 159.) At the evidentiary hearing both attorneys, Sanks and Adams, admitted that they knew there were inconsistencies in the description of the necklace from the search warrant affidavit and the search warrant return. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 6); (Evid. Trial Tr. 9/25/07 at 82–83, 189–190, 281.) Furthermore, defense counsel had been told that the Blue Ash Police Department received this description from the victim's family. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 6); (Evid. Trial Tr. 9/25/07 at 196.) Respondent further contests this claim by asserting that the pendant is difficult to describe and that a description is different from an identification. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 7); (Evid. Trial Tr. 9/25/07 at 104, 166, 195–196.)

Respondent responds to the "custom-crafted" inconsistencies by arguing that the information would not have helped Jones' case due to the unique look of the pendant; the evidence presented that the pendant was

found in the tool box in the trunk of Jones's car, and the pendant was identified at trial as belonging to the victim. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 7.) Therefore, Jones cannot show that it would have been material. *Id*. at 8.

***48** The inconsistencies in description of the pendant would not have been material in this case. While the descriptions of the pendant do vary, particularly when attempting to describe it from memory, when shown the pendant and photos of the victim, multiple people identified this as being the same or identical to the pendant worn by the victim. (Trial Tr. Vol. XIV at 1037); (Trial Tr. Vol. XXVI at 11.) The Court further notes the difficulty of counsel and the Court in describing this particular piece of jewelry for the record during the evidentiary hearing when the item in question was tangibly before them. (Evid. Trial Tr. 9/25/07 at 73, 104–105, 195–196.) Even had defense counsel known of the discrepancies of the description and where it was purchased prior to trial and would have used a different strategy on cross-examination, when confronted with the pendant and the photos, there would have been a positive identification. Likewise, it seems unlikely that defense counsel would have attempted to subpoena the victim's family (noting that her friends and family resided *outside* of the State of Ohio, and therefore outside of subpoena range) to have them testify on direct as to their inconsistent descriptions the pendant, which was most likely due to flawed memories, only to have them make a positive identification when shown the pendant on cross-examination by the State. This sub-claim is without merit and relief on its should be denied.

2. Complaints of Guests about Intruders

Next Jones asserts that *Brady* evidence in the form of complaints from hotel guests about intruders was withheld from him. As a result nothing was presented to the jurors regarding other criminal activity that may have occurred at the hotel the night/day of the murder. (Traverse, Doc. No. 144 at 87.) He specifically cites to questionnaires sent out by Blue Ash Police Department. Some of the responses indicate telephones being out of order, breach of security protocol, many people reporting that they heard screams, maintenance people trying to gain access without properly identifying themselves, and a man that seemed "out of place." *Id.* "These incidents point toward a gang operating in the hotelwhich contradicts the Government theory that Petitioner was the culprit." (Traverse, Doc. No. 144 at 90.)

In looking at the evidence before it the Court is at a loss to find anything like a "gang" operation. The Court notes that the questionnaire responses regarding hearing screams on the morning of September 3, the vast majority, if not all, corresponded with the time that Schub and Kaplan returned to their room and discovered Nathan. It is not disputed that Schub screamed. The other information reported in the questionnaires-people "out of place," non-working telephones, etc.—are not sufficient to undermine confidence in the outcome of Jones's case. When discussed at the evidentiary hearing, defense counsel could only speculate that they would have liked to have had this information so they could follow up with the interviewees and see if they could get any more information. (Evid. Trial Tr. 9/25/07 at 101, 112, 118, 227–238.) Evidence is material only if there is a reasonable probability that, had the evidence been disclosed to the defense, the result of the proceeding would have been different. A 'reasonable probability' is a probability sufficient to undermine confidence in the outcome." *United States v. Bagley,* 473 U.S. 667, 683, 105 S.Ct. 3375, 87 L.Ed.2d 481 (1985).

3. Potential Witnesses

***49** Petitioner alleges statements given by hotel employees Ryan Norman and Demetrius Williams and by hotel guest Robyn Williams contradicted evidence presented at trial and therefore should have been considered *Brady* material and turned over to defense counsel. (Traverse, Doc. No. 144 at 90.) In his statement Norman stated that he saw "a dark skinned male wearing a brown shirt" with a Caucasian man outside of the room; that they then separated and went in different directions. *Id.; citing* (Doc. No. 126, Expansion Disc, Prosecutor's Files at 1508–09, 1711–12.) Jones contends that he did not fit this description, and Norman, as a fellow hotel employee, knew Jones and would not have confused him with someone else. (Traverse, Doc. No. 144 at 90.) Additionally, the statement given by Demetrius Williams on September 3rd, also referenced an African–American male and Caucasian male near the victim's room. (Traverse, Doc. No. 144 at 91.) Again, he asserts that Williams was familiar with Jones and would not have misidentified him. As for the statement of Ms. Williams, she contacted the Blue Ash Police Department to tell them that at approximately 7:45 on the morning of the murder she noticed a white male in his late 20's walking rapidly toward an exit. (Traverse, Doc. No. 144 at 92.) She noted

that the man was tall, thin in build, wearing dark clothes, and left the hotel parking lot on foot. *Id.* Defense counsel testified at the evidentiary hearing that if they had had the information they would have followed up with Mr. Norman, Mr. Williams, and Ms. Williams in an attempt to get a clearer description of the individuals in question, and potentially identify and track them down. (Evid. Trial Tr. 9/25/07 at 99–102, 107–112, 215–216, 223–225.)

Respondent counters Petitioner's argument by stating that the morning of the murder was Norman's first day on the job, and as such, it is conceivable that he may not be able to positively identify Jones. (Reply to Traverse, Doc. No. 82 at 13); (Doc. No. 126, Expansion Disc, Prosecutor's Files at 1711.) Respondent also asserts that the statement made by Demetrius Williams would not have been helpful but rather, may have harmed Jones's case, as Williams also told the police that Jones was "only in comp breakfast for about five minutes-no longer. Does not know why Butch would say he was in comp breakfast when he wasn't." *Id* at 14; citing (Doc. No. 126, Expansion Disc, Prosecutor's File at 1666.) Finally Respondent notes that the statement made by Robyn Williams, that she saw a white male in late 20s walking rapidly toward an exit, would not have changed the outcome of this case.

In order to be *Brady* material, the evidence must be favorable to the accused, either because it is exculpatory, or because it is impeaching; that evidence must have been suppressed by the State, either willfully or inadvertently; and prejudice must have ensued. *Strickler v. Greene,* 527 U.S. 263, 119 S.Ct. 1936, 144 L.Ed.2d 286 (1999). The evidence is material only if there is a reasonable probability that, had the evidence been disclosed to the defense, the result of the proceeding would have been different. A 'reasonable probability' is a probability sufficient to undermine confidence in the outcome." *United States v. Bagley,* 473 U.S. 667, 683, 105 S.Ct. 3375, 87 L.Ed.2d 481 (1985). Jones cannot meet this burden. The statements in questions only show that there were two men in the vicinity of the room around the same time that hotel staff and guests gathered and responded to Schub's screams for help. This information does not undermine the confidence in the result. Likewise, given the fact that the murder occurred in a hotel, the sighting of a man leaving the hotel around the time of the murder does not undermine the confidence in the result.

***50** Next Jones asserts that the list of Embassy Suites Hotel employees and their criminal records as compiled by the police department should have been turned over as *Brady* material. (Traverse, Doc. No. 144 at 92.) For reasons set forth above, this sub-claim is without merit.

Additionally Petitioner observes that in the compilation of the hotel employees, it was noted that some had been subjected to a polygraph examination. (Traverse, Doc. No. 144 at 92.) However, information cannot be considered *Brady* material unless that evidence is or would lead directly to, evidence which would be admissible at trial. *United States v. Phillip,* 948 F.2d 241, 249–50 (6th Cir.1991). The Supreme Court held in *Wood v. Bartholomew* that there was no *Brady* violation when the State failed to disclose to the defendant that a key witness for the State had failed a polygraph exam as the failure of a witness to pass a polygraph test does not constitute admissible evidence under state law. 516 U.S. 1, 116 S.Ct. 7, 133 L.Ed.2d 1 (1995).

To be considered admissible, polygraph results must meet the qualifications adopted by Ohio as articulated in *State v. Valdez,* 91 Ariz. 274, 371 P.2d 894 (1962):(1) that there is a written stipulation for the admissibility of the results signed by all parties, (2) notwithstanding the stipulation the admissibility of the test results is still within the discretion of the trial judge, (3) that if the graph and expert's opinion is offered into evidence then the opposing party shall have the right to cross-examine the expert concerning his qualifications and training, the conditions under which the test was administered, the limitations of and possibilities for error in the polygraph interrogation technique, and other matters deemed pertinent within the discretion of the trial court, and (4) if the evidence is admitted, the trial judge should instruct the jury that the examiner's testimony does not prove or disprove any element of the crime, but rather is only indicative of whether or not the defendant was telling the truth at the time of the examination. *State v. Souel,* 53 Ohio St.2d 123, 372 N.E.2d 1318 (1978). Results of any polygraph tests would not have been admissible in this case as there is no evidence of a written stipulation between the parties allowing for such admission. Furthermore, even assuming that the parties did stipulate to the admittance and the test administrator was available for cross-examination, the decision whether or not to admit such results would still be discretionary with the trial judge. This portion of the *Brady* claim is without merit.

4. Hepatitis

Next Petitioner argues that the Coroner's report showing that the victim, Rhoda Nathan, had tested positive for hepatitis was *Brady* material. (Petition, Doc. No. 15 at 44);(Traverse, Doc. No. 144 at 93.) During the evidentiary hearing, Attorney Sanks recalled, "I don't believe we'd received this part [of coroner's report]. My memory is we did not know she had hepatitis. In the coroner's report, generally, what they place in there, the report that we always get from the coroner, at the end would be the lab work that would be done and the lab work, as I recall, the coroner's report that we had, that the lab work was negative." (Evid. Trial Tr. 9/25/07 at 137–138.) Furthermore, it was testified to that defense counsel did not receive the results of the western block test performed on Jones on September 15, 1994, which was negative for hepatitis. *Id.* at 139. Jones argues that this was an important piece of evidence as there was a supposed linkage between the wound to Petitioner's hand and the victim. *Id.* The importance of this material is allegedly further demonstrated by the fact that Jones tested negative for hepatitis. (Traverse, Doc. No. 144 at 93.)

***51** Respondent argues that the reports contained in the Coroner's file that the victim tested positive for hepatitis, and that Jones tested negative, were not *Brady* material. (Respondent's Post–Evidentiary Hearing Brief, Doc. No. 147 at 11.) First Jones had his own expert at trial, Dr. Solomkin, who knew or should have known about the matters of infectious disease testing, including hepatitis. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 12 .) Dr. Solomkin should have had access to the coroner's report prior to trial, and therefore, should have known that the victim tested positive for hepatitis. *Id.* Furthermore, defense counsel and their expert, knew of the State's "fight-bite" theory prior to trial, and during the evidentiary hearing Dr. Solomkin stated that he had been hired to determine if the *eikenella* bacteria that was found in Jones's hand wound was conclusive evidence that the injury resulted from a human bite. *Id.;* (Evid. Trial Tr. 9/24/07 at 11–12.) Because the defense team had the information as to the fight bite theory and the coroner's report, Dr. Solomkin could have considered what other types of infectious agents Jones may have been exposed to. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 12.) As nothing has been presented to the contrary, Respondent argues that it can only be assumed that Dr. Solomkin thought such line of inquiry would not be beneficial to the defense. *Id.*

Additionally, Respondent argues that Jones cannot show that this information was material to the outcome of his case. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 13.) Specifically, defense counsel could not have legitimately refuted the State's "fight-bite" theory by arguing that if he contracted *eikenella* from the victim, then he would have also contracted hepatitis from her, as a person does not contract everything to which they are exposed. *Id.* at 14. Furthermore, defense counsel refuted the State's claim that Jones contracted *eikenella* from Nathan by emphasizing the gap in the State's evidence, that the victim herself was never tested, and thus did not test positive, as being a carrier of *eikenella. Id.;* (Trial Tr. Vol. XIX at 1777.) Additionally, Respondent notes that the report clearly states that hepatitis "becomes detectable after the incubation state of the virus which generally lasts 4–12 weeks after initial exposure." If one assumed Jones was bitten by Nathan on September 3, 1994, and his own hepatitis test was done 12 days later, then testing was performed during the incubation period, prior to becoming detectable. (Reply to Traverse, Doc. No. 82 at 16); (Respondent's Post–Evidentiary Hearing Brief, Doc No. 147 at 11.) Finally, Respondent argues that the jury did not focus on the medical information during its deliberations. (Respondent's Post–Evidentiary Brief, Doc. No. 147 at 14.) This argument is supported by the fact that the State was not able to establish that Nathan had *eikenella,* so "the jury certainly would not have been persuaded by the argument that, if Jones contracted *eikenella* from Rhoda, he would have also contracted hepatitis from her ..." *Id.*

***52** This claim is without merit. The search warrant affidavit did in fact reference a "fight bite" wound, putting put defense counsel on notice as to the State's theory. (Evid. Trial Tr. 9/25/07 at 125 .) Counsel was aware of Jones's hand infection and consulted an expert as to potential causes. They had received both the medical records on Jones and the coroner's report. (Evid. Trial Tr. 9/25/07 at 76, 123–124, 151.) In fact, there was testimony given during the evidentiary hearing by attorney Sanks that after they received the coroner's report "we went up and interviewed the coroner who did the post and we talked to him quite at length about the report and what he found and why he made his decisions that he made." *Id.* at 136. However, the Court goes on to note that Sanks

did not recall knowing that the victim had tested positive for hepatitis. *Id.* at 137. "In the coroner's report, generally, what they place in there, the report that we always get from the coroner, at the end would be the lab work that would be done and the lab work, as I recall, the coroner's report that we had, that the lab work was negative." *Id.* at 137–138. The copy of the coroner's report appearing in the evidentiary hearing exhibits and on the disc to expand both have the lab work portion showing that the victim tested positive for hepatitis. (Doc. No. 126, Motion H.R. 7 Record Expansion). As for Petitioner's claim that he should have been informed that he had tested negative, this evidence is not material, as he himself was tested within the incubation period. This sub-claim is without merit.

Fourth Ground for Relief

Mr. Jones's defense counsel were ineffective when they failed to adequately investigate and prepare to confront state's witness, Dr. McDonough, and when they failed to effectively prepare their own expert, Dr. Solomkin, regarding Mr. Jones's hand injury and the nature of *Eikenella Corrodens.*

A. Dr. Solomkin thoroughly refutes McDonough's opinions and renders McDonough's testimony constitutionally unreliable.

B. No foundational facts for Dr. McDonough's opinion about whether Mr. Jones or Mrs. Nathan were infected with *Eikenella.*

C. Failure to confront with evidence that Ohio's Bureau of Worker's Compensation paid Mr. Jones's claim based on Dr. McDonough's records.

The governing standard for effective assistance of counsel is found in *Strickland v. Washington,* 466 U.S. 668, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984), and quoted at length above. To show ineffective assistance of trial counsel, Petitioner must be able to show that counsel's performance was deficient. *Id.* It must be evaluated for "reasonableness under prevailing professional norms." *Id.* Next, Petitioner must be able to show that he was prejudiced by the ineffectiveness of counsel. *Id.* at 680. Prejudice results when a defendant is deprived of a fair trial. *Id.* To demonstrate prejudice a petitioner must show that there is a reasonable probability that, but for the unprofessional errors, the result of the proceeding would have been different. *Id.* at 698. "A reasonable probability is a probability sufficient to undermine confidence in the outcome." *Id.; See also Darden v. Wainwright,* 477 U.S. 168, 106 S.Ct. 2464, 91 L.Ed.2d 144 (1986); *Wong v. Money,* 142 F.3d 313, 319 (6th Cir.1998); *Blackburn v. Foltz,* 828 F.2d 1177 (6th Cir.1987). *See generally* Annotation, 26 ALR Fed 218.

A. Dr. Solomkin thoroughly refutes McDonough's opinions and renders McDonough's testimony constitutionally unreliable.

***53** Jones asserts that his counsel were ineffective in that they were not properly prepared to confront the claims made for prosecution by Dr. McDonough. (Petition, Doc. No. 15 at 47.) Specifically, Dr. McDonough's claims that the nature of the hand injury reveals that it had been caused by striking another person in the mouth, and that it was infected with *eikenella corrodens,* which further corroborated his conclusion it was fight bite wound. (Traverse, Doc. No. 144 at 96.) Respondent counters that this claim was raised as the seventh ground for relief in post-conviction proceedings and that the state court held it to be barred by the doctrine of *res judicata* and as such it is now procedurally defaulted. (Return of Writ, Doc. No. 16 at 141.) The state appeals court wrote:

A. Sixth Claim—Dr. McDonough's Testimony

In his sixth claim, Jones contends that his trial counsel was ineffective for failing to object to the testimony of Jones's physician, Dr. McDonough, who testified on behalf of the state. This claim is overruled on the authority of *State v. Jones.* 90 Ohio St.3d 403, 739 N.E.2d 300.

B. Seventh and Thirty—Third ClaimFailure to Investigate and Properly Prepare Cross–Examination

In his seventh claim for relief, Jones argues that he was denied effective assistance because his trial counsel failed to properly prepare for cross-examination of Dr. McDonough, in part by failing to effectively utilize Dr. Solomkin. In his thirty-third claim, Jones contends that trial counsel was ineffective for failing to make a reasonable investigation as a basis for making strategic decisions about medical information admitted at trial once they learned that Dr. McDonough was being called as a state's witness. The trial court concluded that both claims were barred by *res judicata.*

In support of his claims below, Jones filed the affidavit of Dr. Solomkin. The affidavit contained allegations of serious mistakes and flaws in Dr. McDonough's testimony about *eikenella corrodens,* its frequency, its many potential sources, and Dr. McDonough's characterization of Jones's wound as one caused by his hand violently striking another's mouth. It also related the extent to which Jones's attorney was unfamiliar with basic medical science when he questioned Dr. Solomkin.

Jones also supplied the affidavit of Shank, who stated that counsel had failed to adequately challenge the state's theory of the case, failed to prepare for the admissibility of Jones's medical records, and failed to object to McDonough's testimony and the admission of Jones's medical records; and the affidavit of Adams, who stated that she did not speak to Dr. Solomkin prior to the day of his deposition, that the other attorney had obtained him, and that the other attorney had told her that he had provided Dr. Solomkin with Jones's medical reports before the morning of the deposition. Adams's affidavit further stated that she was not aware of the other attorney's failure to prepare Dr. Solomkin until she read the affidavit.

***54** Jones also supplied the affidavit of an Ohio assistance public defender with the materials from one of Jones's trial counsel's file attached. He also provided his own affidavit in which he objected to the use of Dr. McDonough's testimony.

The evidence presented either was available at the time of trial, was cumulative to what was presented at trial, failed to meet the minimum level of cogency, failed to advance his claims, or failed to show that Jones could not have raised this claim on direct appeal. Thus, Jones's claims are barred by *res judicata.*

State v. Jones, 2000 WL 1886307 *8 (Ohio 1st Dist 2000).

This sub-claim is procedurally defaulted. There was a state procedural rule in place, to which Petitioner failed to comply. *Maupin v. Smith,* 785 F.2d 135, 138 (6th Cir.1986). This claim was based on the record and could have been presented in direct appeal. Ohio's criminal *res judicata* doctrine is an adequate and independent state ground of decision, actually enforced against Petitioner by the Ohio courts. However, Jones's presented these sub-claims as portions of his Motion to Reopen under Ohio App. R. 26(B). The Court must, therefore, examine the merits of the underlying claim to the extent necessary to determine whether the state court's opinion on ineffective assistance of appellate counsel is entitled to deference.

Jones asserts counsel's ineffectiveness in their failure to present a defense against the State's medical expert in regard to Jones's hand wound. (Traverse, Doc. No. 144 at 95.) In addition to their failure to confront Dr. McDonough's testimony, counsel were allegedly also ineffective in their failure to prepare defense expert Dr. Solomkin properly. *Id.* Jones also asserts that despite defense counsel's shortcomings, it was the trial court's responsibility to act as a "gatekeeper" and it should not have allowed the majority's of the State's expert witnesses testimony as it was inherently unreliable. *Id.*

It is asserted that defense counsel failed to prepare to confront Dr. McDonough on two central themes: his statement that Jones sustained a hand injury, the nature of which shows that the injury had been caused by Jones striking another person in the mouth, a "fight bite" injury; and the assertion that the wound was infected with *eikenella corrodens,* which according to Dr. McDonough further corroborated the conclusion that this was a fight bite, as this bacteria is found in dental plaque. (Traverse, Doc. No. 144 at 96.) Jones told Dr. McDonough that he injured his hand on the dumpster and then again while moving tables. *Id.* Jones repeated a similar account of events to an investigating officer. *Id.* Therefore, the testimony from Dr. McDonough as to the wound being a fight bite was in direct conflict with what he had been told by his patient. *Id.*

Petitioner asserts that defense counsel lacked a proper knowledge base as to the science behind *eikenella.* (Evid. Trial Tr. 9/24/07 at 41–42.) In support for his claim of counsel's ineffectiveness, Jones references the affidavit and in court testimony of Dr. Solomkin to enumerate the ways in which they could have more effectively challenged Dr. McDonough and could have made his own testimony more effective.[9] (Traverse, Doc. No. 144 at 97); (Evid. Trial Tr. 9/24/07.) Some of these include: Dr. McDonough's opinions were not medically reliable and should not have been given to the jury for consideration; Dr. McDonough was not an expert in the area of infectious disease; Dr. McDonough based his opinion of the "rarity" of *eikenella corrodens* on his own personal surgical experience as opposed to an independent

and larger sample; Dr. McDonough's testimony as to the hand to mouth inoculation of *eikenella corrodens* into the hand wound should have been challenged; information of recent reports that the *eikenella corrodens* bacteria has the ability to produce infections at low inoculation concentrations should have been presented; Dr. McDonough's comment that the bacteria is usually found in dental plaque and not in saliva is incorrect; Dr. McDonough represented in his testimony that Jones's own sample did not contain the *eikenella* flora, however he had been given massive doses of antibiotics which may have cleansed his system of the bacteria; Dr. McDonough presented a prejudicial and irrelevant slide show; while it is unknown if the victim had *eikenella corrodens* approximately one third of the population does have this bacteria; the notion that a person who injures themself and then sucks on the wound not being able to infect themselves was erroneous; Dr. McDonough used speculative conclusions to justify each other, the circular reasoning being, "this is a bite wound because *eikenella* is present and *eikenella* is present because this is a bite wound"; Dr. McDonough was simply speaking and acting as an agent for the State. (Traverse, Doc. No. 144 at 99–101); (Evid. Trial Tr. 9/24/07.)

9 Dr. Solomkin testified through video deposition but testified during a deposition that he would have rearranged his schedule to appear live if he had more notice. (Traverse, Doc. No. 144 at 97); (Evid. Trial Tr. 9/24/07 at 12–13, 43, 48–49.)

***55** Respondent argues this claim is without merit. (Return of Writ, Doc. No. 16 at 141.) The State's expert did give an opinion that Jones's hand injury was a fight bite, resulting from striking someone in the mouth. *Id.* However, defense counsel presented an expert who rebutted this testimony. *Id.* Furthermore, defense counsel was able to elicit testimony from both experts that the bacteria could exist in places other than the human mouth, thus bolstering the defense that the infection was a result of left over food items coming in contact with the open wound. *Id.* Dr. Solomkin also testified to the fact that it is possible for someone to contract the infection by putting the wound in their own mouth. *Id.* Counsel was effective in their cross-examination and preparation of the expert witnesses.

The Court finds this sub-claim to be without merit. Defense counsel effectively cross-examined the State's expert witness as to his area of expertise and his frame of reference for recognizing this type of infection. (Trial Tr. Vol. XIV at 1007, 1029.) They also posed questions as to the origin of *eikenella corrodens,* possible methods of inoculation, and the prevalence of this bacteria among the general population. (*Id.* at 1019, 1021, 1024, 1026.) Defense counsel also challenged whether it was possible that the wound was the result of something other than a fight bite. (*Id.* at 1014–1016.) Furthermore, during cross-examination defense counsel elicited testimony that it may be possible for someone to inoculate themself, if they had *eikenella* in their oral cavity and licked or sucked their open wound. (*Id.* at 1019, 1024.) Defense counsel also presented their own expert, theories, and defense. Dr. Solomkin's testimony confronted Dr. McDonough's assertion that this was a fight bite. Dr. Solomkin stated that due to the "linear laceration" and lack of distinguishing characteristics, it is impossible to tell what caused this wound. (Trial Tr. Vol. XXIX at 9, 17–18, 25); *see also* (Evid. Trial Tr. 9/24/07 at 39.) It may be consistent with a bite, or with falling on a piece of metal. (Trial Tr. Vol. XXIX at 9, 17–18, 25); *see also* (Evid. Trial Tr. 9/24/07 at 39.) Likewise, he contested that *eikenella* is only found in dental plaque by stating it is found throughout the gastrointestinal tract, including in saliva and in the periodontal area. (Trial Tr. Vol. XXIX at 10, 12, 21); (Trial Tr. Vol. XIV at 1000–1001); *see also* (Evid. Trial Tr. 9/24/07 at 15–17.) Dr. Solomkin also provided testimony as to the fact that *eikenella* is common, found in approximately one third of people. (Trial Tr. Vol. XXIX at 12, 21); (Evid. Hrg. Tr. 9/24/07 at 36.) He also gave his opinion that *eikenella* can live outside the body for a variable length of time, possibly several days, making it possible that if someone had an open wound and came in contact with discarded food items or eating utensils that had the *eikenella* bacteria, the person may become inoculated. (Trial Tr. Vol. XXIX at 11, 25–26.) Finally, he affirmed that it would be possible to colonize yourself if you had the bacteria in your mouth and licked or sucked on an open wound. (*Id.* at 22, 26); (Evid. Trial Tr. 9/24/07 at 39, 54.) Counsel were effective in their cross-examination of the State's witness as well as in the presentation of their own expert. This sub-claim is without merit.

B. No foundational facts for Dr. McDonough's opinion about whether Mr. Jones or Mrs. Nathan were infected with *Eikenella.*

***56** Next Petitioner argues his counsel's ineffectiveness in their failure to contest that the State failed to lay proper

foundational facts that the victim had *eikenella corrodens.* (Petition, Doc. No. 15 at 51); (Traverse, Doc. No. 144 at 102.) "This failure rendered inadmissible all of the testimony and argument pertaining to Dr. McDonough's claim that Mr. Jones's hand wound was infected with that bacterium." (Traverse, Doc. No. 144 at 102.) Regardless of this fact, Dr. McDonough was permitted to testify at length that Jones's infection was from a bacteria found in the human oral cavity and transmitted through fight bites. *Id.* Defense counsel were ineffective in their failure to impeach the reliability and credibility of Dr. McDonough's testimony. *Id.* Counsel also failed to cross-examine Dr. McDonough on Defendant's exhibit 6, a laboratory document detailing the analysis of culture from Jones's hand wound, which reported "moderate probable Eikenella species." (Petition, Doc. No. 15 at 52.) Counsel also should have questioned Dr. McDonough on the results of Jones's oral culture, which when tested on October 19, after a course of antibiotics, tested negative for *eikenella corrodens. Id.*

For reasons set forth in the previous sub-claim, this sub-claim is without merit. Dr. McDonough's testimony was admissible and defense counsel was given a thorough opportunity to cross-examine him as well as present testimony from their own expert witness. This Court also notes that there was testimony presented as to the effects of antibiotics on *eikenella* from both experts. (Trial Tr. Vol. XIV at 1024–1025); (Trial Tr. Vol. XXIX at 13–14.)

C. Failure to confront with evidence that Ohio's Bureau of Worker's Compensation paid Mr. Jones's claim based on Dr. McDonough's records.

In his next sub-claim Jones is alleging that defense counsel were ineffective in their failure to present evidence that his Workers' Compensation claim was paid. (Petition, Doc. No. 15 at 53–54.) "No matter what the prosecution did to attack Mr. Jones's version of the injury, the simple and powerful fact remained that the Bureau of Workers' Compensation honored Mr. Jones's claim. This basic fact would have proven that another branch of Government-other than the prosecution-had evaluated the same evidence and found it credible. Moreover, McDonough's own medical records formed the basis for the Workers' Compensation claim." (Traverse, Doc. No. 144 at 105.) Jones additionally argues that the doctor should have alerted the Bureau of Workers' Compensation if he believed Jones was defrauding them. Finally, he argues that Dr. McDonough should have informed law enforcement if he believed this was an injury resulting from violence. (Traverse, Doc. No. 144 at 105.) Considering this claim on appeal from denial of post-conviction relief, the Hamilton County Court of Appeals wrote:

> *P. Thirty–Fourth Claim—Failure to Prepare*
>
> In his thirty-fourth claim, Jones argues that trial counsel failed to adequately prepare for Dr. McDonough's testimony and failed to obtain and use documents generated by the Bureau of Workers' Compensation. According to Jones, his trial counsel could have used the documents to demonstrate that the bureau had viewed his evidence as credible, because it honored Jones's claim of a work-related injury to his hand. Also, the documents could have been used to confront McDonough on why he had not alerted the Bureau of Workers' Compensation that Jones was committing a fraud. To substantiate this claim, Jones provided the same evidence used to support his thirty-third claim, except that the documents attached to the assistant public defender's affidavit were the workers' compensation documents.
>
> ***57** The decision not to use the documents did not rise to the level of ineffective assistance. Jones's claim, at best, provided the existence of an alternative tactical theory. The fact that a different trial tactic "might have improved the defense does not show ineffective assistance of counsel." As we have concluded in our analysis of Jones's thirty-third claim, the evidence outside the record failed to defeat the application of *res judicata.* As to the documents from the Bureau of Workers' Compensation, such evidence failed to demonstrate ineffective assistance of counsel.

State v. Jones, 2000 WL 1886307 *13 (Ohio 1st Dist 2000).

Respondent contends that the above decision is not contrary to nor an unreasonable application of federal law. (Return of Writ, Doc. No. 16 at 143.) Jones made several inconsistent statements as to how he injured his hand. *Id.* Furthermore, the employees listed as witnesses to his accident, testified under oath that they did not actually see Jones injure his hand. *Id.* (Trial Tr. Vol. XIV at 1041, 1111–1112); (Trial Tr. Vol. XVI at 1523). Respondent argues that Jones has failed to meet the *Strickland* standard.

Petitioner's claim is without merit. Defense counsel were not ineffective in their failure to present the workers' compensation claim information, nor in their failure to use it to impeach Dr. McDonough's testimony. Jones cannot establish that had this information been introduced that the outcome of his hearing would have been different. To the contrary, it may have further highlighted the various inconsistent statements given by Jones to others as to how he injured his hand. Additionally, there was testimony from various people listed as "witnesses" to the event on the workers' compensation claim form that they did *not* in fact see Jones injure his hand. (Trial Tr. Vol. XIV at 1041, 1111–1112); (Trial Tr. Vol. XVI at 1521–1523.) Therefore, he is unable to show that he was prejudiced as a result of his counsel not presenting the workers' compensation information. This claim is without merit.

Fifth Ground for Relief

Mr. Jones's trial counsel violated his right to effective assistance of counsel by failing to effectively investigate, discover, research, and utilize exculpatory and impeachment evidence and legal arguments which would have seriously undermined the prosecution's ability to carry its burden of proof and procure a death sentence.

A. Defense Counsel failed to adequately investigate and prepare to confront key medical testimony from state's witness Dr. McDonough, and when they failed to effectively prepare their own expert, Dr. Solomkin.

B. Failure to Investigate History of Crimes at Embassy Suites Hotel

C. Failure to Investigate a Pair of Shoes the Prosecution tied to Mr. Jones

D. Failure to Adequately Investigate an Alternate Suspect Theory

E. Failure to Investigate a Fiber Found in Mr. Jones's Hand Wound

F. Failure to Utilize an Opportunity for Ongoing Investigation During Trial

***58** (Petition, Doc. No. 15 at 56.)

This claim must also be evaluated under the *Strickland* standard. Specifically, this Court must decide if the state court's opinion on this claim was an objectively unreasonable application of *Strickland.*

A. Defense Counsel failed to adequately investigate and prepare to confront key medical testimony from state's witness Dr. McDonough, and when they failed to effectively prepare their own expert, Dr. Solomkin.

Petitioner's first sub-claim argues that counsel were ineffective in their failure to investigate the medical issues, and prepare to confront the State's expert witness on cross-examination. (Petition, Doc. No. 15 at 56.) Ineffectiveness is also alleged in their failure to effectively prepare their own expert witness. *Id*. Respondent alleges that this claim is procedurally defaulted as it was brought before the state courts in post-conviction relief proceedings, but was held to be barred by *res judicata.* (Return of Writ, Doc. No. 16 at 141.) This sub-claim is essentially the same as the previous ground for relief. For the reasons set forth above, this sub-claim is procedurally defaulted and in the alternative without merit.

B. Failure to Investigate History of Crimes at Embassy Suites Hotel

This claim was addressed previously as a prosecutorial misconduct claim. For reasons set forth in that analysis, counsel were not ineffective. *See supra* Third Ground for Relief.

C. Failure to Investigate a Pair of Shoes the Prosecution tied to Mr. Jones

In his next sub-claim, Jones alleges ineffectiveness in counsel's failure to investigate a specific pair of shoes that were taken as a result of a search warrant. (Petition, Doc. No. 15 at 57); (Traverse, Doc. No. 144 at 110.) Jones contends that his counsel were ineffective in their failure to rebut the State's claim that he was the owner of the brown shoes and was wearing these shoes on the day of the crime. *Id.* Additionally, he alleges that his counsel improperly stipulated that the shoes belonged to him. *Id.* Jones asserts that had counsel been effective and performed a reasonable investigation then it would have revealed that the Embassy Suites Hotel dress code required that its employees wear black shoes, and therefore, he must have been wearing black shoes on the day of the murder. *Id.*

Respondent asserts that this claim was raised during post-conviction relief proceedings and addressed on the merits. (Return of Writ, Doc. No. 16 at 139.) The state court held:

> Jones asserts in his sixteenth claim that trial counsel were ineffective because they stipulated to the fact that the brown shoes found in his friend's home belonged to him. To substantiate this claim, he provided to the court below his own affidavit, in which he stated that the shoes were not his, and that he had so informed counsel at trial. Shank's affidavit concluded that Jones's counsel were ineffective in this regard.
>
> ***59** The stipulation in question did not state that the shoes belonged to Jones. It stated instead that they were taken from him as a result of the execution of a search warrant and that testing revealed no blood or blood products. The testimony at trial was that some bruises on the victim's body corresponded to the heel of the shoes, but not to the extent that the similarity excluded all other shoes. The testimony of Jones's "common-law" wife was that the shoes did not belong to Jones, and that he did not own brown shoes. Jones failed to provide evidence supporting substantive grounds for relief.

State v. Jones, 2000 WL 1886307 *10 (Ohio 1st Dist 2000).

This Court agrees with the rationale of the State court. Counsel were not ineffective because of this stipulation. The actual stipulation did not go to the ownership of the shoes, but rather stated that the shoes had been taken from Jones as a result of a search warrant executed at the home of Metcalfe. (Trial Tr. Vol. XIX at 1724); (Return of Writ, Doc. No. 16 at 139.) Additionally, any trial testimony regarding the shoes worked in Jones's benefit. Testimony was given that while bruise patterns were consistent with this type of shoe, it could not be determined that they were made by these particular shoes to the exclusion of others. (Trial Tr. Vol. XIII at 895–897.) Furthermore, there was testimony that the shoes were taken to be tested for blood, and that the results were negative. (Trial Tr. Vol. XIII at 941–942); (Trial Tr. Vol. XV at 1148, 1170, 1198–1200, 1229.) Finally, as to ownership, Yvonne Kinnard, Jones's wife, testified that she did not recognize the shoes as belonging to Jones as he owned black shoes, not brown. (Trial Tr. Vol. XVII at 1654.) Jones was not prejudiced as a result of this stipulation.

D. Failure to Adequately Investigate an Alternate Suspect Theory

Next Jones asserts that his counsel were ineffective in their failure to investigate other possible suspects, including Bill McCall. (Petition, Doc. No. 15 at 57–58); (Traverse, Doc. No. 144 at 113.) With proper investigation into the "alternative suspect theory" used by defense at trial, counsel would have realized that the theory could be "easily and thoroughly shot down," as demonstrated by the State's rebuttal testimony to the defense's attempt to shift suspicion to Bill McCall. (Traverse, Doc. No. 144 at 114.) Jones contends that this failure allowed for the State to cast doubt on his entire case. *Id.*

Respondent concedes this claim was raised in post-conviction relief proceedings. (Return of Writ, Doc. No. 16 at 138–139.) The state courts held that this claim was barred by *res judicata* as the "evidence outside the record" provided by Jones did not provide a substantive claim. *State v. Jones,* 2000 WL 1886307 * 8 (Ohio 1st Dist 2000). Respondent notes that the claim was also raised as an underlying claim for ineffective assistance of appellate counsel.

***60** This claim is procedurally defaulted. In applying *Maupin,* there was a state procedural rule in place, to which Petitioner failed to comply. *Maupin v. Smith,* 785 F.2d 135, 138 (6th Cir.1986) This claim was based on the record and should have been presented in direct appeal. Ohio's criminal *res judicata* doctrine is an adequate and independent state ground of decision, actually enforced against Petitioner by the Ohio courts. However, Jones's presented these sub-claims as portions of his Motion to Reopen under Rule 26(B). Therefore, some examination of the merits of Jones's underlying sub-claim is therefore necessary to evaluate the state court's decision on the ineffective assistance of appellate counsel claim.

The Court finds this sub-claim is without merit. Jones did not demonstrate that this was not a reasonable trial strategy or that counsel failed to investigate. While it is obvious from the record that the State called McCall as a rebuttal witness to contest defense's theory that he should have been considered a suspect, the actual defense theory employed, that there were other employees at the hotel that should have been considered but were not, remained a reasonable trial strategy. The Court notes that counsel made mention of several individuals who should have been considered and during closing argument reiterated to

the jurors that they were not mentioned as a way to shift the blame, but rather to demonstrate that the case was not investigated as thoroughly as it should have been and that the Blue Ash Police failed to investigate all possible suspects. (Trial Tr. Vol. XIX at 1756, 1784–1785.)

E. Failure to Investigate a Fiber Found in Mr. Jones's Hand Wound

Next Jones advances his sub-claim that counsel were ineffective in their failure to investigate a blue fiber found in his hand wound. (Petition, Doc. No. 15 at 58.) Respondent notes that this claim was raised on petition for post-conviction relief. (Return of Writ, Doc. No. 16 at 142.) To further this claim, Jones supplied an affidavit by attorney Adele Shank, an experienced capital case litigator, who stated that it was necessary for counsel to hire an expert on this issue. *Id.;* (Return of Writ, Doc. No. 16, Apx. Vol. IX at 190–196.) The state court held that the claim was speculative and insufficient to demonstrate ineffective assistance, stating that:

> In his seventeenth claim for relief, Jones argues that his trial counsel were ineffective for failing to move for the appointment of an independent expert to analyze the fiber found in his wound. He contends that such an expert might have provided an alternative explanation of *eikenella corrodens.* In the court below, Jones proffered Shank's affidavit, which stated that such an expert was necessary. The court concluded that this claim was *res judicata.* We disagree. But Jones has still failed to demonstrate ineffective assistance of counsel. The evidence outside the record does not meaningfully demonstrate that the choice not to move for the appointment of an expert constituted ineffective assistance. The evidence is speculative.

***61** *State v. Jones,* 2000 WL 1886307 *11 (Ohio 1st Dist 2000). As the last state court to address this claim did so on the merits, this Court may consider the claim as well. The Strickland standard applies.

Jones speculates that "the fiber at issue provided a missed opportunity to present the jury with an alternative explanation for the hand injury and infection." (Traverse, Doc. No. 144 at 116.) He argues that if the fiber was found to be inconsistent with any fibers found in Nathan's hotel room then it could have bolstered his own account of how he hurt his hand. *Id.*

Respondent argues that this claim is without merit as Jones is attempting to second guess defense counsel's strategy. (Return of Writ, Doc. No. 16 at 142.) Furthermore, Respondent notes that the blue fiber was only mentioned briefly by Dr. McDonough. *Id.* There was no detailed testimony nor pathology report. *Id.* Jones's argument does not show that the failure to have an expert on this issue deprived him of a fair trial. *Id.*

This claim is without merit. Jones fails to demonstrate how the outcome of trial would have been different had defense counsel requested an expert to examine the fiber. The blue fiber was mentioned in passing, "we found purulent material [in the wound], and there was a little blue piece of fiber in there." (Trial Tr. Vol. XIV at 1022–1023.) The fiber was sent to the lab for a pathology report, and Dr. McDonough was unsure what had happened to the fiber after it was sent to the lab. *Id.* at 1023, 1031.

Jones has not shown that an expert to further investigate this fiber would have changed the outcome of his trial. Testimony was presented to give Jones's account as to how he injured his hand at work (moving the dance floor, moving tables, and falling on the stairs near the dumpster) and defense expert, Dr. Solomkin, likewise testified as to an alternative means of inoculation of the wound in that it is possible to transmit *eikenella* by licking or sucking on a wound or by having an open wound come in contact with infected food. (Trial Tr. Vol. XIV at 983, 991, 1043, 1067–1068, 1094); (Trial Tr. Vol. XV at 1343, 1345); (Trial Tr. Vol. XVI at 1451, 1524); (Trial Tr. Vol XVII at 1649); (Trial Tr. Vol. XXIX at 11, 22–26.) Additionally, the jury heard that after injuring his hand Jones had it wrapped. (Trial Tr. Vol. XIV at 1043–1044); (Trial Tr. Vol. XVI at 1451, 1454, 1462); (Trial Tr. Vol. XVII at 1649.) This "wrap" which has been described as everything from a bandage to "wrapped in something" could account for the presence of the blue fiber. Furthermore, there is no evidence that the mention of the blue fiber in the wound impacted jury deliberations or that it deprived Jones of a fair trial. Finally, no expert evidence was offered in

the habeas evidentiary hearing to support the speculation about what could have been shown at trial.

F. Failure to Utilize an Opportunity for Ongoing Investigation During Trial

***62** Next Jones alleges that his counsel were ineffective in their failure to effectively use Ohio Rule of Criminal Procedure Rule 16(B)(1)(g) to review any prior statements of prosecution witnesses immediately following their direct examination. (Petition, Doc. No. 15 at 58); (Traverse, Doc. No. 144 at 118.) If they had done so they would allegedly have been able to cross-examine the witnesses as to their prior inconsistent statements. (Traverse, Doc. No. 144 at 118.) He further alleges that there was no objectively sound reason for his counsel to bypass this important tool for confrontation, yet more often than not they failed to make this request, and when they did make a request they did not insist on their right to take part in the trial court's inspection of the statement. *Id. citing* (Trial Tr. Vol. XIII at 871); (Trial Tr. Vol. XIV at 1006, 1042, 1056, 1071, 1112); (Trial Tr. Vol. XV at 1151, 1238; 1312, 1361); (Trial Tr. Vol. XVI at 1407.) Jones argues that this failure deprived him of effective counsel and of his constitutional right to confront witnesses. (Traverse, Doc. No. 144 at 118.)

Respondent notes that this claim was raised during post-conviction relief proceedings where the court held that it was based on the record, and was therefore barred by *res judicata;* it is also said to lack merit (Return of Writ, Doc. No. 16 at 144.) Not requesting the statements may have been trial strategy and defense counsel effectively cross-examined the State's witnesses. *Id.* Furthermore, Respondent argues even if counsel had used the rule more frequently, there is no reasonable probability that the outcome of the trial would have been different. *Id.*

Because this sub-claim was based on the record, absent a showing of cause and prejudice, it is procedurally defaulted. In the alternative, it is also without merit. In Jones's skeleton *Strickland* argument, he alleges that counsel's decision not to use this rule fell below a reasonable standard, however, he does not show, nor does he attempt to show, prejudice. *Strickland v. Washington,* 466 U.S. 668, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984); (Traverse, Doc. No. 144 at 118.) He states only that they could have been more effective in their cross-examination if they had asked to see the prior statements. After a full review of the record, this Court finds that counsel were effective in their cross-examination of the State's witnesses, and that Jones has not sufficiently shown that had they more frequently used the Ohio rule, that there was a reasonable probability that the outcome of his case would have been different.

Sixth Ground for Relief

Elwood Jones was denied the right to counsel, when Attorney Sanks abdicated his role as defense counsel.

In his sixth ground for relief, Jones makes the argument that defense counsel Sanks failed to actively advocate his case. (Petition, Doc. No. 15 at 60.) Specifically, he alleges that Sanks expressed to both Jones and Jones's family his contempt for Jones's prior criminal record and his alleged actions in this case. *Id.* Petitioner has withdrawn this ground for relief. (Traverse, Doc. No. 144 at 119.)

Seventh Ground for Relief

***63** Mr. Jones's constitutional right to a fair, non-arbitrary and reliable capital sentencing hearing were violated by his counsel's failure to investigate mitigation evidence and the trial court's refusal to permit the presentation of a viable "residual doubt" mitigation argument.

In his seventh ground for relief, Jones asserts that counsel were ineffective in their failure to effectively investigate, identify, and present to Jones all available mitigation evidence. (Petition, Doc. No. 15 at 61); (Traverse, Doc. No. 144 at 119–121.) He argues he was not made aware of his options when he choose to waive mitigation and present only a residual doubt theory. *Id.* Additionally, he argues trial court error in its refusal to instruct the jury on residual doubt. *Id.* at 62.

Respondent concedes this claim was presented on direct appeal. (Return of Writ, Doc. No. 16 at 40.) It was again presented in his post-conviction petition where the court of appeals held that Jones did not advance sufficient evidence to demonstrate ineffective assistance. (Return of Writ, Doc. No. 16 at 146.) Petitioner has withdrawn the portion of this claim pertaining to trial counsel error. (Traverse, Doc. No. 144 at 120.) On direct appeal the Ohio Supreme Court held:

In his fourth proposition of law, appellant alleges ineffective assistance based on counsel's failure to present available mitigation evidence. At the beginning

of the mitigation hearing, defense counsel informed the court that appellant had always maintained he was innocent in the murder of Nathan and that the only mitigation he wanted counsel to present was residual doubt. The trial judge specifically asked appellant if that was accurate, and appellant replied, "Yes, it is, Your Honor." On the second day of the mitigation hearing, the court informed the defense that it would not instruct the jury on residual doubt based on the decision in Garner, 74 Ohio St.3d at 56–57, 656 N.E.2d at 632.

As we noted recently in *State v. Ashworth (1999)*, 85 Ohio St.3d 56, 63, 706 N.E.2d 1231, 1238, even if the court attempted to require an attorney to present mitigating evidence, it cannot force an unwilling defendant to provide that evidence to his attorney. Moreover, where the defendant does not want to present mitigating evidence, no societal interest counterbalances the defendant's right to control his own defense. *State v. Tyler (1990)*, 50 Ohio St.3d 24, 28, 553 N.E.2d 576, 584.

Here, nothing suggests that appellant was not competent to forgo presenting any mitigating evidence. Nor did appellant ever indicate a change of heart after the court's refusal to instruct on residual doubt. In fact, at his sentencing hearing appellant again maintained his innocent and indicated that he had twice refused to accept a plea bargain on manslaughter. In light of all the foregoing, counsel were not ineffective for failing to present available mitigating evidence. We overrule appellant's fourth proposition.

***64** *State v. Jones*, 90 Ohio St.3d 403, 411, 739 N.E.2d 300, 311 (2000).

For reasons set forth in the Ninth Ground for Relief, the portion pertaining to trial court error for failure to give an instruction on residual doubt is without merit. *See infra* Ninth Ground for Relief. The trial court permitted Jones to present mitigation evidence, including that of residual doubt. *Franklin v. Lynaugh*, 487 U.S. 164, 173, 108 S.Ct. 2320, 101 L.Ed.2d 155 (1988) *quoting Lockhart v. McCree*, 476 U.S. 162, 180–182, 106 S.Ct. 1758, 90 L.Ed.2d 137 (1986). However, the United States Supreme Court has never required a court to instruct on residual doubt. *Franklin v. Lynaugh*, 487 U.S. 164, 108 S.Ct. 2320, 101 L.Ed.2d 155 (1988).

Eighth Ground for Relief

Systematic flaws in Hamilton County's methods for selecting grand jurors, grand jury forepersons, and petit jury venires yielded racial, gender, and socio-economic biases inimical to Mr. Jones's constitutional rights. His rights were further violated when the prosecution excluded all African–Americans from his jury. Mr. Jones's counsel failed to effectively challenge these unconstitutional systemic factors; failed to raise an obvious challenge; failed to conduct an effective voir dire; and failed to raise effective challenges to venire persons.

A. The composition of the Grand Jury that indicted Mr. Jones failed to comply with constitutional requirements.

B. The selection of the foreperson of the Grand Jury that indicted Mr. Jones failed to comply with constitutional requirements.

C. The composition of the Petit Jury venire and the jurors empaneled for Mr. Jones's trial failed to comply with constitutional requirements.

D. The prosecution's use of peremptory challenges to exclude all African–American citizens from Mr. Jones's Petit Jury creates a strong presumption of racial animus.

E. Defense counsel failed to conduct an effective voir dire, and they failed to challenge a biased juror.

F. Defense counsel violated Mr. Jones's constitutional rights by failing to raise an obvious *Batson* challenge, and by failing to challenge the systemic deficiencies in the way Hamilton County selects Grand Jurors, Grand Jury forepersons, and the venire for Petit Juries.

Petitioner Jones alleges that the jury selection process used in Hamilton County results in petit and grand juries that are biased geographically, racially, culturally, and socio-economically. (Petition, Doc. No. 15 at 63.) He contends that an over-representation of residents from the northwestern part of Hamilton County skewed his grand jury causing it to be over-populated by white members of the middle and upper class. *Id*. Additionally, he alleges that the composition of his petit jury venire likewise failed to comply with constitutional requirements. *Id.* at 64.

Jones raised this claim for the first time during his post-conviction relief proceedings. The court of appeals held:

> In his second and third claims, Jones argues that the process by which Hamilton County selects grand jurors and the forepersons of grand juries in capital cases is biased geographically, racially, culturally, and socio-economically. In his fourth claim, he contends that the prospective jury panel for his capital case was not a representative cross-section of the community because only six of the sixty prospective jurors were African American.
>
> ***65** To support his claims below, Jones presented an affidavit of a criminal investigator who provided a list that she had compiled in 1994 of twenty-one Hamilton County grand-jury forepersons who had returned capital indictments. Of that total, nineteen were "white," and the race of the remaining two was not identified. Jones also supplied the list of grand jurors and their addresses from 1985 through 1990, the deposition testimony of a Hamilton County common pleas judge, who stated that the administrative judge had the responsibility of selecting forepersons in Hamilton County, two photographs and various documents concerning Jones, including minor-misdemeanor citations and correspondence concerning employment (all which Jones had in a briefcase located in the trunk of his case), and completed jury questionnaires provided by potential jurors in his case. This claim is barred by *res judicata,* as it could have been raised at trial or on direct appeal. The evidence outside the record either is irrelevant to Jones's claim, was available at the time of Jones's trial, or fails to present sufficient operative facts to demonstrate that Hamilton County systemically excludes distinctive groups in the community from serving as grand jurors.

State v. Jones, 2000 WL 1886307 at *3 (Ohio App. 1st Dist.2000).

A. The composition of the Grand Jury that indicted Mr. Jones failed to comply with constitutional requirements.

The selection of the foreperson of the Grand Jury that indicted Mr. Jones failed to comply with constitutional requirements.

This claim is procedurally defaulted. Pursuant to Ohio R.Crim. P. 6(B) and Ohio R.Crim. P. 12(B), the proper time to challenge the makeup to the grand jury and its foreperson is before trial. Ohio R.Crim. P. 6(B) provides that the challenge must be made by a motion to dismiss the indictment. Ohio R.Crim. P. 12(B) further requires that an objection based on the indictment be made before the trial. *Smith v. Anderson* further instructs that a claim of this nature must be brought on direct appeal and failing to do so results in the Petitioner's effectively waiving it. 104 F.Supp.2d 773, 849 (S.D.Ohio 2000), affirmed in *Smith v. Mitchell,* 348 F.3d 177 (6th Cir.2003). The state court was correct in its finding that the claim should have been brought on direct appeal. To overcome a bar of *res judicata,* however, a petitioner can provide evidence outside the record. This material must be competent, relevant, material, more than marginally significant, and must advance the claim beyond mere a hypothesis and a desire for further discovery. *State v. Perry,* 10 Ohio St.2d 175, 266 N.E.2d 104 (1967). The evidence provided by Jones was not sufficient to meet this standard. The material submitted with the post-conviction relief petition was available at the time of trial and could have been presented then. Both portions of this claim are procedurally defaulted.

Petitioner seeks to excuse that default by showing ineffective assistance of appellate counsel. To evaluate the court of appeals decision that there was no ineffective assistance of appellate counsel in failing to raise this claim, the Court must examine briefly the merits of the claim. The Supreme Court has set out the following as necessary in making a *prima facie* case of discrimination of grand jury members:

> ***66** In order to show that an equal protection violation has occurred in the context of grand jury selection, the defendant must show that the procedure employed resulted in substantial under representation of his race or the identifiable group to which he belongs. The first step is to establish that the group is one that is a recognizable, distinct class, singled out for different treatment under the laws, as written or applied .... Next the degree of under representation must be proved by comparing the proportion of the group in the

> total population to the proportion called to serve as grand jurors, over a significant period of time .... Finally, ... a selection procedure that is susceptible of abuse or is not racially neutral supports the presumption of discrimination raised by the statistical showing .... Once the defendant has shown substantial under representation of his group, he has made a prima facie case of discriminatory purpose and the burden then shifts to the state to rebut the case.

Castaneda v. Partida, 430 U.S. 482, 494–495, 97 S.Ct. 1272, 51 L.Ed.2d 498 (1977). Petitioner fails to argue how the procedure to select grand jury members results in the under representation of various classes. The compiled lists span a five-year time period ending approximately five years before Petitioner's case went to trial. The lists themselves do not establish the person's racial or socio-economic status. Petitioner has failed to make a *prima facie* case as to discrimination of grand jury members.

The position of the grand jury foreperson is not derived from the Constitution but rather from statutory law for the administrative convenience of the court. In *Hobby* the Court held that any discrimination in the selection of the grand jury foreman, as distinguished from discrimination in the selection of the grand jury itself, does not threaten the interests of the defendant. *Hobby v. United States,* 468 U.S. 339, 344, 104 S.Ct. 3093, 82 L.Ed.2d 260 (1984). The Court based this on the fact that "the role of the foreman of a federal grand jury is not so significant to the administration of justice that discrimination in the appointment of that office impugns the fundamental fairness of the process itself so as to undermine the integrity of the indictment." *Id.* at 345. It concluded that reversal of a criminal defendant's conviction would be an inappropriate remedy as the impact from the violation would play a minor part in federal prosecutions. *Id.* at 350. The role of the foreperson in Ohio is similar to the role of the federal foreperson as discussed in *Hobby v. United States.* Portions of Ohio Rules of Criminal Procedure Rule 6 state:

> A) Summoning grand juries. The judge of the court of common pleas for each county, or the administrative judge of the general division in a multi-judge court of common pleas or a judge designated by him, shall order one of more grand juries to be summoned at such times as the public interest requires. The grand jury shall consist of nine members, including the foreman, plus not more than five alternates.
>
> ***67** * * * *
>
> C) Foreman and deputy foreman. The court may appoint any qualified elector or one of the jurors to be foreman and one of the jurors to be deputy foreman. The foreman shall have power to administer oaths and affirmations and shall sign all indictments. He or another juror designated by him shall keep a record of the number of jurors concurring in the finding of every indictment and shall upon the return of the indictment file the record with the clerk of court, but the record shall not be made public except on order of the court. During the absence or disqualification of the foreman, the deputy foreman shall act as foreman.

Petitioner is not able to establish prejudice. In support of his claim he provides an affidavit of a criminal investigator which states she compiled a list in 1994 of twenty-one former Hamilton County grand-jury forepersons who had returned capital indictments, of these twenty-one, nineteen were Caucasian; and a deposition of a judge stating that forepersons are appointed. Without more, Petitioner cannot demonstrate a pattern or practice within Hamilton County to show that forepersons are selected in a discriminatory manner or results in a discriminatory application. This claim is without merit. Because it has no merit, it was not ineffective assistance of appellate counsel to fail to raise it on direct appeal and the Ohio Court of Appeals decision to that effect is neither contrary to nor an unreasonable application of clearly established federal law.

> C. The composition of the Petit Jury venire and the jurors empaneled for Mr. Jones's trial failed to comply with constitutional requirements.

In his next sub-claim Petitioner asserts that he was denied his constitutional rights because the petit jury venire and jurors failed to comply with constitutional requirements. (Petition, Doc. No. 15 at 64.)

Respondent argues that the sub-claim is procedurally defaulted as Petitioner failed to raise it on direct appeal. (Return of Writ, Doc. No. 16 at 94.) Jones did raise

the sub-claim in post-conviction relief, however, the state courts held it to be barred by Ohio's doctrine of criminal *res judicata. Id.* Alternatively, Respondent argues the claim is without merit as the Constitution does not entitle a defendant to a jury made up of a particular racial composition, but rather "requires only that the venires from which juries are selected do not cause a systemic exclusion of any particular racial group in the community," *Id.* at 96; *Taylor v. Louisiana,* 419 U.S. 522, 538, 95 S.Ct. 692, 42 L.Ed.2d 690 (1975); *Duren v. Missouri,* 439 U.S. 357, 99 S.Ct. 664, 58 L.Ed.2d 579 (1979); *Fay v. New York,* 332 U.S. 261, 284, 67 S.Ct. 1613, 91 L.Ed. 2043 (1947).

This claim is procedurally defaulted. In applying *Maupin,* there was a state procedural rule in place, to which Petitioner failed to comply. *Maupin v. Smith,* 785 F.2d 135, 138 (6th Cir.1986). This claim was based on the record and should have been presented in direct appeal. Ohio's criminal *res judicata* doctrine is an adequate and independent state ground, actually enforced against Petitioner by the Ohio courts. *Buell v. Mitchell,* 274 F. 3rd 337 (6th Cir.2001); *Coleman v. Mitchell,* 268 F.3d 417 (6th Cir.2001); *Byrd v. Collins,* 209 F.3d 486, 521–22 (6th Cir.2000), *cert. denied* 531U.S. 1082, 531 U.S. 1082, 121 S.Ct. 786, 148 L.Ed.2d 682 (2001); *Rust v. Zent,* 17 F.3d 155, 160–61 (6th Cir.1994); *Van Hook v. Anderson,* 127 F.Supp.2d 899 (S.D.Ohio 2001).

***68** Alternatively, in turning to the merits, it is established U.S. Supreme Court law that:

> It should also be emphasized that in holding that petit juries must be drawn from a source fairly representative of the community we impose no requirement that petit juries actually chosen must mirror the community and reflect the various distinctive groups in the population. Defendants are not entitled to a jury of any particular composition, *Fay v. New York,* 332 U.S. 261, 284, 67 S.Ct. 1613, 91 L.Ed. 2043 (1947); *Apodaca v. Oregon,* 406 U.S. at 416 (plurality opinion); but the jury wheels, pools of names, panels, or venires from which juries are drawn must not systematically exclude distinctive groups in the community and thereby fail to be reasonably representative thereof.

Taylor v. Louisiana, 419 U.S. 522, 538, 95 S.Ct. 692, 42 L.Ed.2d 690 (1975).

To show a *prima facie* violation for a fair cross-section claim, a petitioner must show 1) that the group alleged to be excluded is a "distinctive" group in the community; 2) that the representation of this group in venires from which juries are selected is not fair and reasonable in relation to the number of such persons in the community; and 3) that this underrepresentation is due to systematic exclusion of the group in the jury-selection process. *Taylor v. Louisiana,* 419 U.S. 522, 587, 95 S.Ct. 692, 42 L.Ed.2d 690. Petitioner has not taken any steps to establish the third prong of this test. Additionally, Ohio courts have held that the use of voter registration lists and voter rolls as opposed to driver's license lists does not create a representative cross-section claim. *State v. Fulton,* 57 Ohio St.3d 120, 566 N.E.2d 1195 (1991), *following Duren v. Missouri,* 439 U.S. 357, 364, 99 S.Ct. 664, 58 L.Ed.2d 579 (1979). This sub-claim is without merit.

D. The prosecution's use of peremptory challenges to exclude all African–American citizens from Mr. Jones's Petit Jury creates a strong presumption of racial animus.

In his next sub-claim Petitioner argues that the State improperly used a peremptory challenge to exclude an African–American from his jury in violation of *Batson v. Kentucky,* 476 U.S. 79, 106 S.Ct. 1712, 90 L.Ed.2d 69 (1986).

Respondent argues that this sub-claim is procedurally defaulted as Petitioner failed to object at the proper time and alternatively, is without merit. (Return of Writ, Doc. No. 16 at 94, 97.) During post-conviction relief proceedings, the court held that the evidence *de hors* the record, in the form of questionnaires and various jurors' comments during voir dire, was available at trial and could have been presented then, therefore the claim is barred by *res judicata. Id.; State v. Jones,* 2000 WL 1886307 at *3 (Ohio App. 1st Dist.2000).

Thus Ohio's criminal *res judicata* doctrine is was enforced against Petitioner by the Ohio courts. While this claim is procedurally defaulted, Petitioner contests the default

by arguing cause and prejudice in his trial counsel's ineffectiveness to object during voir dire and in appellate counsel's failure to raise the claim on direct appeal. (Traverse, Doc. No. 144 at 132.) He did present it as an underlying claim in his ineffective assistance of appellate counsel claim, and to the extent necessary to review the Court of Appeals decision on that claim, this Court will look at the merits.

***69** It is clearly established United States Supreme Court law that the State may not exercise its [peremptory] challenges in violation of the Equal Protection Clause. It is impermissible to use the challenges to exclude from the jury minorities "for reasons wholly unrelated to the outcome of the particular case on trial" or to deny "the same right and opportunity to participate in the administration of justice enjoyed by the white population." *Batson v. Kentucky,* 476 U.S. 79, 91, 106 S.Ct. 1712, 90 L.Ed.2d 69 (1986) *quoting Swain v. Alabama,* 380 U.S. 202, 224, 85 S.Ct. 824, 13 L.Ed.2d 759 (1965). As with any equal protection claim, the defendant who alleges the discrimination has the burden of establishing "the existence of purposeful discrimination." *Id.; Whitus v. Georgia,* 385 U.S. 545, 550, 87 S.Ct. 643, 17 L.Ed.2d 599 (1967) *citing Tarrance v. Florida,* 188 U.S. 519, 23 S.Ct. 402, 47 L.Ed. 572 (1903).

A state criminal defendant can establish a *prima facie* case of purposeful racial discrimination in the selection of jurors solely by proof of peremptory challenges to exclude members of the defendant's race. *Batson v. Kentucky,* 476 U.S. 79, 106 S.Ct. 1712, 90 L.Ed.2d 69 (1986). A trial court must use a three-step process to evaluate a *Batson* claim. First, the opponent must make a *prima facie* showing that the proponent of the strike has exercised a peremptory challenge on the basis of race. The burden then shifts to the proponent to articulate a race-neutral reason for the challenge. Finally, the trial court must determine if the opponent has carried his burden of proving purposeful discrimination. *Purkett v. Elem,* 514 U.S. 765, 768, 115 S.Ct. 1769, 131 L.Ed.2d 834 (1995); *Hernandez v. New York,* 500 U.S. 352, 111 S.Ct. 1859, 114 L.Ed.2d 395 (1991).

To make a *prima facie* showing, a defendant must show that he is a member of a cognizable racial group, that a challenge has been exercised to remove a venireperson of the same race, and any additional facts and circumstances from which an inference could be drawn that the prosecutor had used the peremptory challenge in a race-based manner. *Batson,* 476 U.S. at 79. The defendant is entitled to rely on the fact that the peremptory challenge process is one in which those who are of a mind to discriminate on the basis of race are able to do so. *Id.* A trial judge's conclusion that the challenge was race-neutral must be upheld unless it is clearly erroneous. *Hernandez; supra; United States v. Tucker,* 90 F.3d 1135, 1142 (6th Cir.1996); *United States v. Peete,* 919 F.2d 1168, 1179 (6th Cir.1990).

Specifically, Petitioner alleges that Ms. Blair, an African–American woman, was in the third alternate juror position when the State waived its final two peremptory challenges. Defense counsel then exercised two challenges, thus moving Ms. Blair into the position of first alternate juror. "The State's inaction and the defense's action placed Juror Blair into a position as first alternate juror, rather than gaining a position on the petit jury. If the State had exercised either remaining peremptory challenge, Juror Blair would have been placed on the petit jury without an additional opportunity for the State to exercise a challenge against her." (Traverse, Doc. No. 144 at 134.) Petitioner continues by alleging that "once placed into the position as first alternate juror, the State exercised a peremptory challenge against Juror Blair." *Id.* Defense counsel failed to raise a *Batson* objection to the State's challenge. This caused Juror Brewer to be in the position of first alternate juror, and ultimately, be moved into a position as a juror when another juror was unable to remain for the sentencing determination. *Id.*

***70** The Court notes that there is no rule requiring that either party exercise all their peremptory challenges. Ohio Criminal Rule 24(D) states that "each party peremptorily may challenge ... six prospective jurors in capital cases...." [10] The parties *may* use, not *must* use.

10 Ohio Revised Code § 2945.21(A)(2) states that "in capital cases in which there is only one defendant, each party, in addition to the challenges for cause authorized by law, may peremptorily challenge twelve of the jurors. If there is more than one defendant, each defendant may peremptorily challenge the same number of jurors as if he were the sole defendant." The adoption of Criminal Rule 24 displaces the prior statute. Regardless, for the proposition raised above, again the language of "may" is used as opposed to "must."

Furthermore, Petitioner cannot establish a *prima facie* case of intentional discrimination. Jones offers no additional evidence or circumstances surrounding the challenge to show that it was motivated by race. While he alleges that "it appears that the prosecution used its peremptory challenges in a manner designed to prevent any African–American from serving on Mr. Jones's Petit Jury," after a reviewing the record, it appears that Ms. Blair was the *only* African–American in the venire to be questioned before a jury was in place. Therefore, a pattern of the State's challenges against a particular race in this case cannot be established. Of the sixty venire members, six were African–American, two were excused prior to individual voir dire. The potential jurors were then questioned numerically, and Ms. Blair, juror number 39, was in a position to be questioned before a jury was decided upon, whereas the others were not. It is also noted that Ms. Blair was thoroughly questioned by both the State and defense counsel in the same manner as the other jurors. Her answers stated that she had a brother that was a deputy and that she was a victim of crime, her mother had been shot. (Trial Tr. XII at 765–776, 798.) Petitioner has failed to show other facts that give rise to the inference that the Prosecutor's use of this peremptory challenge was racially based. This sub-claim is without merit.

E. Defense counsel failed to conduct an effective voir dire, and they failed to challenge a biased juror.

In his next sub-claim, Petitioner argues that his counsel were ineffective in their failure to rehabilitate jurors who opposed the death penalty and in their failure to challenge for cause a juror who may have been biased as a result of his law enforcement training. (Petition, Doc. No. 15 at 66.) Petitioner raised this claim on direct appeal where the Ohio Supreme Court held that:

> In his third proposition of law, appellant contends that counsel failed to attempt rehabilitation of jurors who opposed the death penalty during voir dire. Appellant also asserts that counsel failed to challenge for cause a juror (Hamilton), who admitted that he might be unable to put aside his experience as a police officer and objectively consider the evidence presented. Appellant's claims of ineffective assistance in this context are unfounded.
>
> Appellant cites six jurors whom counsel should have rehabilitated: Chavez, Noe, Cripe, Baker, Brooks, and Cook. However, voir dire revealed that all were unalterably opposed to the death penalty and that their strong views "would prevent or substantially impair the performance" of their duties as jurors. *See State v. Rogers* (1985), 17 Ohio St.3d 174, 17 OBR 414, 478 N.E.2d 984, paragraph three of the syllabus. Moreover, the failure to probe views of jurors who were excused for cause under death qualification, does not constitute ineffective assistance, since trial counsel is in a better position to determine if jurors can be rehabilitated. *Bradley,* 42 Ohio St.3d at 143, 538 N.E.2d at 381.
>
> ***71** With respect to the failure to challenge Juror Hamilton for cause, the transcript reveals no ground that counsel could have successfully asserted as a challenge. Hamilton indicated that he would follow the law: "I may not agree with it but it's my job and I have to do it." Therefore, we overrule appellant's third proposition.

State v. Jones, 90 Ohio St.3d 403, 411, 739 N.E.2d 300, 311 (2000).

Petitioner argues that counsel's failure to rehabilitate jurors who expressed a preference for life imprisonment over the death penalty would result in a jury that was stacked in favor of death. (Petition, Doc. No. 15 at 66.) This argument is misleading as the potential jurors did not express a preference for one sentence over the other, but rather adamantly stated they could not impose a sentence of death. As the United States Supreme Court held in *Witherspoon v. Illinois,* the proper inquiry on voir dire is not whether the prospective juror is opposed to the death penalty, but rather whether their religious, moral, or conscientious objections would preclude them from following the instructions of the court. 391 U.S. 510, 521–522, 88 S.Ct. 1770, 20 L.Ed.2d 776 (1968). Thus, it is proper to exclude for cause a prospective juror who indicates that either they could not vote for capital punishment under any circumstances or that they would be hesitant to do so. *Morgan v. Illinois,* 504 U.S. 719, 728, 112 S.Ct. 2222, 119 L.Ed.2d 492 (1992); *Lockhart v. McCree,* 504 U.S. 719, 728, 112 S.Ct. 2222, 119 L.Ed.2d 492, (1986) (holding that juror can be removed for cause for a hesitancy to impose a death sentence); *see also Luckett v. Kemna,* 203 F.3d 1052, 1054–5 (8th Cir.2000); *see further Gosier v. Welborn,* 175 F.3d 504, 509–10 (7th Cir.1999); *Keel v. French,* 162 F.3d 263, 271 (4th Cir.1998). When a trial judge excuses a juror as to whom the judge has a definite impression that the prospective juror will be unable to faithfully apply the law, that decision is entitled

to deference. *State v. Beuke,* 38 Ohio St.3d 29, 38, 526 N.E.2d 274, 284–85, *citing Wainwright v. Witt,* 469 U.S. 412, 105 S.Ct. 844, 83 L.Ed.2d 841 (1985).

This Court has reviewed the voir dire in connection with the jurors in question; Chavez, Noe, Cripe, Baker, Brooks, and Cook. (Trial Tr. Vol. XI at 510–515; 517–519; 627–629); (Trial Tr. Vol. XII at 671–673; 682–687.) Each of the potential jurors were questioned by both the judge and counsel. While the reasons for opposition to the death penalty varied—from religious and moral opposition to personal events, the six potential jurors all had a general opposition which would seriously impair his or her ability to recommend a death sentence even under appropriate circumstances. The Court concludes counsel were not ineffective in their failure to rehabilitate these jurors. The state court decision affirming their removal for cause was not an unreasonable applications of clearly established federal law. *See State v. Jones,* 1998 WL 542713 at *3 (Ohio App. 1 Dist.1998); *State v. Jones,* 90 Ohio St.3d 403, 411, 739 N.E.2d 300, 311 (2000). This claim is therefore without merit.

***72** In the second portion of this sub-claim, Petitioner argues that counsel were ineffective in their failure to challenge for cause a juror who admitted it would be difficult for him to put his law enforcement training aside and judge the case based on the evidence. (Petition, Doc. No. 15 at 66–67.) The challenged exchange is as follows:

> Ms. Adams: As an officer you received training in how to investigate crime scenes?
>
> Prospective Juror Hamilton: Yes, ma'am.
>
> Ms. Adams: And how to investigate allegations? Prospective Juror Hamilton: (Nodding.)
>
> Ms. Adams: You understand that that's special training that you can't bring into the jury with you?
>
> Prospective Juror Hamilton: Yes, ma'am
>
> Ms. Adams: We are asking you to leave outside a large part of what you do every single day.
>
> Prospective Juror Hamilton: Right. Ms. Adams: Can you do that?
>
> Prospective Juror Hamilton: I would hope I could. I can't say for sure that I would. I'm sure that there would be sometimes that I would think more into it than what was being said maybe. But I would hope that I could. To be quite honest I can [sic] can't give you a yes or no answer.
>
> Ms. Adams: Well, that's honest. I can appreciate that.

(Trial Tr. Vol. XII at 789.)

The ultimate question is whether a juror swore that he or she could set aside any opinion that he might hold and decide the case on the evidence and whether that juror's protestation of impartiality should have been believed. *Patton v. Yount,* 467 U.S. 1025, 1036, 104 S.Ct. 2885, 81 L.Ed.2d 847 (1984). "The question of whether a trial court has seated a fair and impartial jury is a factual one, involving an assessment of credibility." *Gall v. Parker,* 231 F.3d 265 (6th Cir.2000), *citing Patton.* A trial court's finding of impartiality is a factual determination entitled to 28 U.S.C. 2254(e)'s presumption of correctness. *Dennis v. Mitchell,* 354 F.3d 511, 520 (6th Cir.2003). Juror Hamilton told the trial court that he would follow the law, and make his decision based on the evidence presented and the instructions as given by the court. (Trial Tr. Vol. XII at 786, 790.) As such counsel was not ineffective in their failure to challenge for cause.

> F. Defense counsel violated Mr. Jones's constitutional rights by failing to raise an obvious *Batson* challenge, and by failing to challenge the systemic deficiencies in the way Hamilton County selects Grand Jurors, Grand Jury forepersons, and the venire for Petit Juries.

For reasons set forth in the first, second, and third sub-claim of this ground for relief, these sub-claims are without merit. Counsel were not ineffective.

Ninth Ground for Relief

> Multiple errors in the jury instructions at both phases of Mr. Jones's trial violated his constitutional rights to a fair trial, effective assistance of counsel, and to be free from an arbitrary and capricious death sentence.

In his Ninth Ground for Relief, Petitioner advances numerous claims of constitutional violations as a result of improper instructions to the jury. (Petition, Doc. No. 15 at 68.) The sub-claims are set forth below:

*73 1. The instructions improperly allowed the jury to presume purpose from the manner in which the killing was done.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 141.)

2. The "gist of the offense" definition for "purpose" improperly relieved the State of its burden to prove each element of the aggravated murder offense.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 141.)

3. The instructions to the jury as to cause and foreseeability improperly interjected a civil liability standard that undermined the specific intent requirement of Ohio Rev.Code § 2903.01(B)(D).

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 141.)

4. The instructions improperly allowed the jury to presume knowledge from the facts in evidence, which created a conclusive presumption of mens rea.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 141.)

5. The instructions improperly shifted the burden of proof upon Mr. Jones to disprove the elements of the crime and prove his innocence.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 141.)

6. The jury was improperly instructed that it must consider mitigating factors not raised by Mr. Jones.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 142.)

7. The jury was not properly instructed that it must independently weigh the aggravating circumstances of each count against the mitigating factors. Tr.1959–60; *State v. Cooey,* 46 Ohio St.3d 20, 544 N.E.2d 895 (1989)

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 142.)

8. The jury was improperly instructed to consider all the evidence admitted at both proceedings when determining Petitioner's sentence.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 142.)

9. The jury was improperly instructed that the nature and circumstances of the offense are equated with the aggravating circumstances.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 142.)

10. The sentencing jurors were not properly informed that they need not be unanimous on a finding of a mitigating factor in order to use it in their weighing process, that they did not have to unanimously find death inappropriate before considering the life sentences; the sentencing jury was improperly instructed that a life sentence recommendation must be unanimous.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 142.)

> 11. Ohio's statutory definition of reasonable doubt is constitutionally infirm because it embodies a standard of proof below that required by the Due Process Clause of the Fourteenth Amendment. The "firmly convinced" language in Ohio's statutory definition of reasonable doubt operates to lower the standard from "proof beyond a reasonable doubt" to "clear and convincing evidence." The "willing to act" language is too lenient to satisfy the stringent Due Process standard for criminal conviction and has been criticized by the United States Supreme Court when used as a component of defining "beyond reasonable doubt."

***74** Respondent does not allege procedural default but rather states that this sub-claim is properly preserved for federal habeas review. (Return of Writ, Doc. No. 16 at 99.) In addressing this claim on direct appeal the Ohio Supreme Court held:

> In his twenty-third proposition of law, appellant asserts that the court's instruction on reasonable doubt based on the definition in R.C. 2901.05(D) constitutes reversible error. However, beginning with *State v. Jenkins* (1984), 15 Ohio St.3d 164, 15 OBR 311, 473 N.E.2d 264, paragraph eight of the syllabus, we have uniformly upheld use of the statutory definition of reasonable doubt in capital case jury instructions. See *e.g., State v. Moore* (1998), 81 Ohio St.3d 22, 37, 689 N.E.2d 1, 15. We overrule appellant's twenty-third proposition.

State v. Jones, 90 Ohio St. 403, 417, 739 N.E.2d 300, 315 (2000); *See also State v. Jones,* 1998 WL 542713 at * 13 (Ohio App. 1st Dist.1998).

The instruction as given by the trial court reads:

> Now, reasonable doubt is present when, after you've carefully considered and compared all the evidence, you cannot say you are firmly convinced of the truth of the charge.
>
> Reasonable doubt is a doubt that is based and [sic] reason and common sense. Reasonable doubt is not mere possible doubt, because everything relating to human affairs or depending on moral evidence is open to some possible or imaginary doubt.
>
> Proof beyond a reasonable doubt is proof of such character that an ordinary person would be willing to rely and act upon it in the most important of his or her own affairs.

(Trial Tr. Vol. XIX at 1833–1834.) Ohio's definitions of reasonable doubt and proof beyond a reasonable doubt as defined in O .R.C. § 2901.05(D) have been upheld by the Sixth Circuit. *Thomas v. Arn,* 704 F.2d 865, 869 (6th Cir.1983); *Scott v. Mitchell,* 209 F.3d 854, 883–884 (6th Cir.2000); *Byrd v. Collins,* 209 F.3d 486, 527 (6th Cir.2000); *Coleman v. Mitchell,* 268 F.3d 417, 436–437 (6th Cir.2001). This sub-claim is therefore without merit; the Ohio Supreme Court's ruling is neither contrary to nor an unreasonable application of clearly established federal law.

> 12. The penalty phase reasonable doubt instruction was constitutionally defective. It said: "reasonable doubt is present when, after you've carefully considered and compared all the evidence, you cannot say you are firmly convinced of the truth of the charge." Tr.1957. The jurors could not by definition have had any reasonable doubt about the sentence based on this definition. They were already firmly convinced of **the truth of the charge,** since they had returned convictions on the death-eligible counts of the indictment. This instruction operated as a mandatory presumption in the state's favor, a presumption which relieved the state of its penalty phase burden of proof. Such presumptions are illegal, and violate the Due Process Clause of the Fourteenth Amendments. *Sandstorm v. Montana,* 442 U.S. 510, 99 S.Ct.

2450, 61 L.Ed.2d 39 (1979); *Francis v. Franklin,* 471 U.S. 307, 105 S.Ct. 1965, 85 L.Ed.2d 344 (1985). Moreover, because these jurors were already firmly convinced of the truth of the "charge" against Elwood Jones, they were compelled to return a death verdict against him at the penalty phase because Ohio Rev.Code 2929.03(D)(2) states that a death sentence "shall" be imposed if the state carries its burden of proof at the mitigation phase. Instructions like these, which make death the mandatory sentence have long been held to offend the Eighth Amendment. *Woodson v. North Carolina* (1976), 428 U.S. 280, 96 S.Ct. 2978, 49 L.Ed.2d 944.

***75** Respondent does not allege procedural default and agrees that this sub-claim is properly preserved for federal habeas review. (Return of Writ, Doc. No. 16 at 99.) In addressing this claim on direct appeal the Ohio Supreme Court held:

> In his twenty-fourth proposition of law, appellant argues that the court erred in using the statutory definition of reasonable doubt during penalty-phase instructions. Admittedly, the trial court's reference to the "truth of the charge" is not the preferred language for a penalty-phase reasonable-doubt instruction. *Moore,* 81 Ohio St.3d at 37, 689 N.E.2d at 15. However, any such error is harmless where the trial court clearly instructs the jury that, before recommending death, it must be convinced beyond a reasonable doubt that the aggravating circumstances outweigh the mitigating factors, and that the prosecution has the burden of proof on the issue. *State v. Taylor* (1997), 78 Ohio St.3d 15, 29–30, 676 N.E.2d 82, 96. Since the trial court clearly instructed the jury in this manner, appellant's twenty-fourth proposition is not well taken.

State v. Jones, 90 Ohio St. 403, 418, 739 N.E.2d 300, 316 (2000); *see also State v. Jones,* 1998 WL 542713 at * 13 (Ohio App. 1st Dist.1998). Though repetition of the phrase "truth of the charge" from the guilt phase instruction is inaccurate, the error is harmless in the context of the full instruction given here. *Coleman v. Mitchell,* 268 F.3d 417, 436 (6th Cir.2001).

> 13. The definition of mitigating factors in Ohio Rev.Code § 2929.04(B)(7) and the jury instructions violates the reliability component of the Eighth Amendment.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 149.)

> 14. The trial court erred when it rejected defense counsel's request for an instruction on residual doubt at the penalty phase of trial. Tr.1912. It also overruled repeated objections to describing the jury's verdict at that phase as a 'recommendation.' Tr. 285, 1915. Defense counsel presented no evidence in mitigation, and argued only residual doubt as a mitigating factor, together with some discussion of the moral and religious implications of imposing a death sentence. Tr. 1890, 1925–1941. The prosecutor repeatedly emphasized the theme that the Judge would instruct the jury on everything that they were permitted to consider, that their oath as jurors limited their consideration to only those factors contained in the instructions, and that they really had little or no discretion in making the sentencing decision. See ex., Tr.1942–1945. This argument, coupled with the judge's refusal to mention residual doubt in his instructions, had the same effect as an instruction not to consider residual doubt, or any other factor not specifically mentioned in the instructions. This violated the United State's Supreme Court's mandate that

> the jury not be prohibited from considering mitigation evidence offered by Mr. Jones for a sentence less than death. It also had the effect of minimizing or lessening the jurors' sense of responsibility for the ultimate sentence, a tactic condemned by the United States Supreme Court.

***76** The first portion of this sub-claim relates to the trial court's failure to give the jurors an instruction on residual doubt during the sentencing phase. Respondent does not allege procedural default and agrees that this sub-claim is properly preserved for federal habeas review. (Return of Writ, Doc. No. 16 at 99.) In addressing this claim on direct appeal the Ohio Supreme Court held:

> In his fourteenth proposition of law, appellant asserts error in the trial court's failure to instruct on residual doubt, which led the state to argue that appellant had forfeited any right to a weighing of aggravating circumstances against mitigating factors, since no mitigating evidence was presented. Appellant further contends that the trial court erred in repeatedly instructing the jury that their verdict was a "recommendation."
>
> Both of these arguments lack merit. Residual doubt is not an acceptable mitigating factor. *State v. McGuire* (1997), 80 Ohio St.3d 390, 686 N.E.2d 1112, syllabus. In addition, use of the term "recommendation" does not diminish the jury's sense of responsibility, accurately reflects Ohio law, and does not constitute error. *State v. Woodward* (1993), 68 Ohio St.3d 70, 77, 623 N.E.2d 75, 80–81. We overrule appellant's fourteenth proposition.

State v. Jones, 90 Ohio St. 403, 418, 739 N.E.2d 300, 316 (2000).

At the time of Jones's trial, the Ohio courts were recognizing residual doubt as a mitigating factor. Shortly thereafter, however, in *State v. McGuire,* 80 Ohio St.3d 390, 686 N.E.2d 1112 (1997), the Ohio Supreme Court explained that:

> Residual or lingering doubt as to the defendant's guilt or innocence is not a factor relevant to the imposition of the death sentence because it has nothing to do with the nature and circumstances of the offense or the history, character, and background of the offender.... Our system requires that the prosecution prove all elements of a crime beyond a reasonable doubt. Therefore, it is illogical to find that the defendant is guilty beyond a reasonable doubt, yet then doubt the certainty of the guilty verdict by recommending mercy in case a mistake has occurred. Residual doubt casts a shadow over the reliability and credibility of our legal system in that it allows the jury to second-guess its verdict of guilt in the separate penalty phase of a murder trial....

Id. at 403, 686 N.E.2d 1112; *See also State v. Garner,* 74 Ohio St.3d 49, 56–57, 656 N.E.2d 623, 632 (1995) (holding that even in jurisdictions recognizing a capital defendant's right to argue residual doubt, that the defendant is not entitled to an instruction on residual doubt); *Coleman v. Mitchell,* 244 F.3d 533, 544 (6th Cir.2001), *quoting State v. McGuire,* 80 Ohio St.3d 390, 686 N.E.2d 1112; *cited approvingly in Buell v. Mitchell,* 274 F.3d 337, 359 (6th Cir.2001). Furthermore, the Ohio Supreme Court actually *rejected* residual doubt as a mitigating factor in *State v. Smith,* 61 Ohio St.3d 284, 297, 574 N.E.2d 510, 521 (1991).

***77** Regardless of whether residual doubt could have been considered as a mitigating factor at the time of Jones' trial, Petitioner fails to show a federal constitutional violation. He attempts to argue a violation under *Lockett v. Ohio* as a result of the trial court's denying his request for this instruction. (Petition, Doc. No. 15 at 70.) The United States Supreme Court, however, has never required a court to instruct on residual doubt. *Lockhart* did not endorse the use of residual doubt in capital proceedings. Rather, it stood for the proposition that "where states are willing to go to allow defendants to capitalize on 'residual doubts' such doubts will inure to the defendant's benefit." *Franklin v. Lynaugh,* 487 U.S. 164, 173, 108 S.Ct. 2320, 101 L.Ed.2d 155 (1988) *quoting Lockhart v. McCree,* 476 U.S. 162, 180–182, 106 S.Ct. 1758, 90 L.Ed.2d 137 (1986). The *Lynaugh* court recognized *Eddings* and *Lockhart* in that a sentencer may not be precluded from considering any aspect of a defendant's character, or record, or circumstances of the offense as mitigating evidence, but

stated that lingering doubt does not fall within any of these aspects:

> Our edict that, in a capital case, " 'the sentencer ... [may] not be precluded from considering, *as a mitigating factor,* any aspect of a defendant's character or record and any of the circumstances of the offense,' " *Eddings v. Oklahoma,* 455 U.S. 104, 110, 102 S.Ct. 869, 71 L.Ed.2d 1 (1982) (quoting *Lockett [v. Ohio*], 438 U.S. [586,] ... 604, 98 S.Ct. 2954, 57 L.Ed.2d 973 [(1978)]), in no way mandates reconsideration by capital juries, in the sentencing phase, of their "residual doubts" over a defendant's guilt. Such lingering doubts are not over any aspect of petitioner's "character," "record," or a "circumstance of the offense." This Court's prior decisions, as we understand them, fail to recognize a constitutional right to have such doubts considered as a mitigating factor.

Franklin v. Lynaugh, 487 U.S. 164, 174, 108 S.Ct. 2320, 101 L.Ed.2d 155 (1988). It is therefore, not constitutionally required that the jury reconsider any of their "residual doubts" during the mitigation phase. *Franklin v. Lynaugh,* 487 U.S. 164, 108 S.Ct. 2320, 101 L.Ed.2d 155 (1988); *Eddings v. Oklahoma,* 455 U.S. 104, 110, 102 S.Ct. 869, 71 L.Ed.2d 1 (1982) and *Lockett v. Ohio,* 438 U.S. 586, 604, 98 S.Ct. 2954, 57 L.Ed.2d 973 (1978).

Even assuming such rights existed, there was no violation in this case. The trial court did not do anything to impair Jones's exercise of his "right" to present residual doubt to the jury. Counsel was permitted to argue and present evidence supporting the existence of residual doubt. (Trial Tr. Vol. XXI at 1898–1900); (Trial Tr. Vol. XXII at 1934, 1939–1940.) Furthermore, while not instructed on residual doubt specifically, the jurors could have considered this under the "catch all" provision as they were instructed they could consider "any other factors that are relevant to the issue of whether the defendant should be sentenced to death." (Trial Tr. Vol. XXII at 1957.) *See supra* Seventh Ground for Relief at 120–121. The state court's decision is not inconsistent with United States Supreme Court law. This sub-claim is without merit.

***78** The next sub-claim pertains to the use of the word "recommendation" in instructing the jurors as to their role in the sentencing process. (Petition, Doc. No. 15 at 70); (Traverse, Doc. No. 144 at 149–152.) In order to make a *Caldwell* violation, the jury instructions must improperly lessen the responsibility of the jurors. The Sixth Circuit has repeatedly upheld the use of the word "recommendation" in the penalty phase instructions. *Mapes v. Coyle,* 171 F.3d 408, 413 (6th Cir.1999); *Byrd v. Collins,* 209 F.3d 486, 527 (6th Cir.2000); *Scott v. Mitchell,* 209 F.3d 854, 877 (6th Cir.2000); *Buell v. Mitchell,* 274 F.3d 337, 352–353 (6th Cir.2001). It is an accurate description of Ohio law. It has been held repeatedly that the jury may make a recommendation to the court that the sentence of death be imposed on the defendant, and that the trial court has the discretion to accept or reject the recommendation of death. Therefore, the final determination of whether or not a sentence of death is appropriate, rests with the court. *Buell v. Mitchell,* 274 F.3d 337, 352–353 (6th Cir.2001). This sub-claim is without merit.

> 15. Defense counsel failed to request and the trial court failed to give a cautionary instruction regarding the weight to be given to Dr. McDonough's testimony in the light of the fact that he lacked expertise in the area of medicine that he testified about.

Petitioner has withdrawn this claim. (Traverse, Doc. No. 144 at 152.)

Tenth Ground for Relief

> Mr. Jones's appellate counsel violated his right to effective assistance of appellate counsel by failing to raise obvious errors, which if raised, would have rendered his conviction and death sentence unreliable. These constitutional violations rendered Mr. Jones's conviction and death sentence unreliable.

In his Tenth Ground for Relief, Jones asserts that his appellate counsel failed to raise arguably meritorious claims on direct appeal, and that this failure constituted ineffective assistance. (Petition, Doc. No. 15 at 72.)

Respondent counters by stating that when Jones presented his motion to reopen to the state courts, the court of appeals held that with the exception of one claim, all alleged errors were trial error and not appellate counsel error. (Return of Writ, Doc. No. 16 at 148); (Return of Writ, Doc. No. 16 Apx. Vol. XV at 191, *State v. Jones,* Hamilton Co.App. No. C–970043) relying on *State v. McNeill,* 83 Ohio St.3d 457, 700 N.E.2d 613, 615 (1998). As a result the court found that Jones had not properly

alleged ineffective assistance of appellate counsel, but even assuming it had been properly raised, Jones failed to state " 'the manner in which the deficiency prejudicially affected the outcome of the appeal,' as required by App. R. 26(B)(2)(d)." (Return of Writ, Doc. No. 16 Apx. Vol. XV at 191, *State v. Jones,* Hamilton Co.App. No. C–970043.) He appealed to the Ohio Supreme Court which applied the *Strickland* standard to assess whether Jones had raised a genuine issue as to ineffective assistance of appellate counsel. The Ohio Supreme Court concurred with the decision of the court of appeals. *State v. Jones,* 91 Ohio St.3d 376, 745 N.E.2d 421 (2001).

***79** Respondent additionally argues that Jones's claim lacks merit. (Return of Writ, Doc. No. 16 at 150.) Even a cursory review of the issues raised in Jones's direct appeal show that appellate counsel raised claims of ineffective assistance of counsel, prosecutorial misconduct, and challenges to the admissibility and sufficiency of the evidence. *Id.* Appellate counsel used their professional judgment to decide which claims to raise, those that seemed to have the best chance of succeeding on appeal, and Jones has not made a showing that the omitted claims were "clearly stronger" than those brought on direct appeal. *Id.* In concluding, Respondent states that Jones has failed to meet the *Strickland* standard by failing to show that his counsel were so deficient that is a reasonable probability that he would not have been convicted and sentenced to death, but for these deficiencies. *Id.*

A criminal defendant is entitled to effective assistance of counsel on appeal as well as at trial. *Evitts v. Lucey,* 469 U.S. 387, 105 S.Ct. 830, 83 L.Ed.2d 821 (1985); *Penson v. Ohio,* 488 U.S. 75, 109 S.Ct. 346, 102 L.Ed.2d 300 (1988). The right to counsel is limited to the first appeal as of right. *Ross v. Moffitt,* 417 U.S. 600, 94 S.Ct. 2437, 41 L.Ed.2d 341 (1974). "In order to succeed on a claim of ineffective assistance of appellate counsel, a petitioner must show errors so serious that counsel was scarcely functioning as counsel at all and that those errors undermine the reliability of the defendant's convictions." *McMeans v. Brigano,* 228 F.3d 674 (6th Cir.2000), *citing Strickland v. Washington,* 466 U.S. 669 (1984); *Rust v. Zent,* 17 F.3d 155, 161–62 (6th Cir.1994); *Smith v. Robbins,* 528 U.S. 259, 285, 120 S.Ct. 746, 145 L.Ed.2d 756 (2000); *Burger v. Kemp,* 483 U.S. 776, 107 S.Ct. 3114, 97 L.Ed.2d 638 (1987).

The attorney need not advance every argument, regardless of merit, urged by the appellant. *Jones v. Barnes,* 463 U.S. 745, 751–52, 103 S.Ct. 3308, 77 L.Ed.2d 987 (1983) ("Experienced advocates since time beyond memory have emphasized the importance of winnowing out weaker arguments on appeal and focusing on one central issue if possible, or at most on a few key issues.") Effective appellate advocacy is rarely characterized by presenting every non-frivolous argument which can be made. *Williams v. Bagley,* 380 F.3d 932, 971 (6th Cir.2004); *See Smith v. Murray,* 477 U.S. 527, 106 S.Ct. 2661, 91 L.Ed.2d 434 (1986). However, failure to raise an issue can amount to ineffective assistance. *McFarland v. Yukins,* 356 F.3d 688 (6th Cir.2004), *citing Joshua v. Dewitt,* 341 F.3d 430, 441 (6th Cir.2003); *Lucas v. O'Dea,* 179 F.3d 412, 419 (6th Cir.1999); and *Mapes v. Coyle,* 171 F.3d 408, 427–29 (6th Cir.1999). Counsel's failure to raise an issue on appeal could only be ineffective assistance if there is a reasonable probability that inclusion of the issue would have changed the result of the appeal. *McFarland v. Yukins,* 356 F.3d 688, 699 (6th Cir.2004), *citing Greer v. Mitchell,* 264 F.3d 663, 676 (6th Cir.2001), *cert. denied,* 535 U.S. 940, 122 S.Ct. 1323, 152 L.Ed.2d 231 (2002). "Counsel's performance is strongly presumed to be effective." *McFarland, quoting Scott v. Mitchell,* 209 F.3d 854, 880 (6th Cir.2000). To prevail on a claim of ineffective assistance of appellate counsel, a petitioner must show that appellate counsel ignored issues which are clearly stronger than those presented. *Smith v. Robbins,* 528 U.S. 259, 288, 120 S.Ct. 746, 145 L.Ed.2d 756 (2000), *quoting Gray v. Greer,* 800 F.2d 644, 646 (7th Cir.1986).

***80** In *Mapes v. Coyle,* 171 F.3d 408 (6th Cir.1999), the court wrote that

> ... the following considerations ought to be taken into account in determining whether an attorney on direct appeal performed reasonably competently.
>
> (1) Were the omitted issues 'significant and obvious'?
>
> (2) Was there arguably contrary authority on the omitted issues?
>
> (3) Were the omitted issues clearly stronger than those presented?
>
> (4) Were the omitted issues objected to at trial?
>
> (5) Were the trial court's rulings subject to deference on appeal?

(6) Did appellate counsel testify in a collateral proceeding as to his appeal strategy and, if so, were the justifications reasonable?

(7) What was appellate counsel's level of experience and expertise?

(8) Did the petitioner and appellate counsel meet and go over possible issues?

(9) Is there evidence that counsel reviewed all the facts?

(10) Were the omitted issues dealt with in other assignments of error?

(11) Was the decision to omit an issue an unreasonable one which only an incompetent attorney would adopt?

Manifestly, this list is not exhaustive, and neither must it produce a correct "score"; we offer these inquiries merely as matters to be considered.

171 F.3d at 427–28 (6th Cir.1999) (citations omitted).

Petitioner's Tenth Ground for Relief reproduces the claims raised in his Murnahan motion. They are considered here seriatim.

> 1. The acts and omissions of Mr. Jones's trial counsel and the trial court's failure to ensure a fair trial violated his rights to effective assistance of counsel, due process, fair trial, confrontation of witnesses, and freedom from cruel and unusual punishment as guaranteed by the Sixth, Eighth and Fourteenth amendments of the United States Constitution and Article I, Sections 2, 9, 10 and 16 of the Ohio Constitution.

This claim contained the sub-claims of ineffectiveness of trial counsel in their failure to: object to statements that Jones had requested an attorney during questioning; that Jones had consulted with an attorney; defense counsel failed to effectively use Ohio R.Crim. P. 16(B)(1)(g) to review any statements of the State's witnesses; that they failed to obtain their own pathologist to assist in the defense; that they failed to effectively prepare their expert witness, Dr. Solomkin; failed to properly investigate their own blame-shifting theory; failed to object to the trial court's reference to Jones's prior conviction; failed to object to the State's references to Jones's prior convictions; were ineffective for informing the prospective jurors and later the seated jurors as to Jones's prior conviction; failed to object to the admission of the briefcase into evidence; failed to object to the prosecutor's closing argument when he referenced facts not in evidence (link between bruise pattern and objects, that Jones confronted Friend in an angry manner, that victim tested positive for *eikenella*), shifted the burden of proof; commented on defense counsel's failure to conduct forensic tests, expressed a personal opinion as to Jones's guilt and vouched for the State's case; failed to effectively object to the slide show used by the State's expert; failed to object when the State discussed Jones's indictment; and failed to object to double hearsay in Officer Lilley's testimony. (Petition, Doc. No. 15 at 73–76.)

> ***81** 2. The prosecutor's misconduct during Mr. Jones's capital trial and the trial court's failure to ensure a fair trial was prejudicial and denied Mr. Jones a fair trial in violation of the Fifth, Sixth, Eighth and Fourteenth amendments to the U.S. Constitution, Article I, Sections 5, 9, 10 and 16 of the Ohio Constitution, *Berger v. United States,* 295 U.S. 78, 55 S.Ct. 629, 79 L.Ed. 1314 (1935) and *Donnelly v. DeChristoforo,* 416 U.S. 637, 94 S.Ct. 1868, 40 L.Ed.2d 431 (1974).

Under this portion, Petitioner included the following as sub-claims: improper comment that Jones had requested an attorney; improperly attacked the credibility of Johnson by eliciting evidence of his criminal history; improperly commented during opening statements that Jones had a history of aggravated burglary convictions; argued facts not in evidence during closing arguments (link between bruise pattern and objects, that Jones confronted Friend in an angry manner, that victim tested positive for *eikenella*), shifted the burden of proof, commented on defense counsel's failure to conduct forensic tests on the objects in the State's control, expressed a personal opinion as to Jones's guilt, and

improperly vouched for the State's case. (Petition, Doc. No. 15 at 76–77.)

> 3. The trial court's admission of purported "expert" opinion testimony that failed to meet the threshold of opinions held to a reasonable degree of medical and/or scientific certainty, and which was at best based on drawing inferences from inferences which ultimately had no factual basis in the record, and Mr. Jones's trial counsel's failure to effective challenge the admissibility of this testimony, violated Mr. Jones's rights to effective assistance of counsel, due process, fair trial, confrontation of witnesses, equal protection and freedom from cruel and unusual punishment as guaranteed by the Sixth, Eighth and Fourteenth Amendments of the United States Constitution, Article I, Sections 2, 9, 10 and 16 of the Ohio Constitution.

This claim contains the following sub-claims, the trial court erred in: admitting testimony from purported experts who were permitted to render opinions that fell below the standard of "to a reasonable degree of scientific or medical certainty"; the appellate court misapplied *State v. D'Ambrosio,* 67 Ohio St.3d 185, 191, 616 N.E.2d 909 (1993); the testimony regarding the purported comparison between certain physical objects and the bruise pattern had no direct factual basis in the record; and the court permitted the testimony of an officer as an expert on blood splatter evidence. (Petition, Doc. No. 15 at 77–79.)

> 4. The trial court committed numerous errors in instructing the jury in the [sic] both the culpability phase and the penalty phase of Mr. Jones's capital trial, which errors were compounded by defense counsel's ineffective failure to raise timely and/or proper objections and counsel's failure to request proper jury instructions, all of which prejudiced Mr. Jones, denied him a fair trial, and violated the Fifth, Sixth, Eighth, and Fourteenth Amendments of the United States Constitution and Article I, Sections 2, 5, 9, 10 and 16 of the Ohio constitution.

***82** The sub-claim under the trial court errors claim include various alleged errors in instructing the jury: jury instructions improperly allowed the jury to presume the purpose from the manner in which the killing was done; the "gist of the offense" definition for "purpose" relieved the State of its burden to prove each element of the aggravated murder offense; the instruction as to cause and foreseeability improperly interjected a civil liability standard that undermined the specific intent requirement; improperly allowed the jury to presume knowledge from the facts in evidence, which created a conclusive *mens rea;* improperly shifted the burden of proof to Jones to disprove the elements of the crime and prove his innocence; improperly told the jury their verdict was merely a recommendation; improperly instructed that the jury must consider mitigating factors not raised by Jones; did not properly instruct the jury that it need not unanimously find death inappropriate before considering life sentences; did not properly instruct the jury that it must independently weigh the aggravating circumstances of each count against the mitigating factors; improperly instructed the jury to consider all the evidence admitted at both proceedings when determining Jones's sentence; improperly instructed that the nature and circumstances of the offense are equated with the aggravating circumstances; did not properly inform the jury that it need not be unanimous on a finding of a mitigating factor in order to use it in their weighing process; improperly instructed that a life sentence recommendation must be unanimous; the instructions at sentencing improperly placed the jury's focus on what it previously found in terms of reasonable doubt at the guilt phase; the definition of mitigating factors in the Ohio Revised Code violated the reliability component of the Eighth Amendment; and defense counsel failed to request a cautionary instruction regarding the weight to be given to Dr. McDonough's testimony in light of the fact that he lacked expertise in the area of medicine to which he testified. (Petition, Doc. No. 15 at 79–81.)

5. The trial court erred when it denied Mr. Jones the right to present the testimony of Mr. Vickers which prejudiced Mr. Jones and denied him a fair trial, his right to compulsory process, his right to confront the state's case against him, and violated the Fifth, Sixth, Eighth, and Fourteenth Amendments of the United States Constitution and Article I, Sections 2, 5, 9, 10 and 16 of the Ohio Constitution.

6. Mr. Jones's indictment was returned by an improperly constituted grand jury, including defects in (1) the biased process used to select the foremen of grand juries, (2) the manner and adequacy of the presentation of evidence which yields capital indictments with a discriminatory intent and impact on racial minorities in violation of the Fifth, Sixth, Eighth and Fourteenth Amendments of the United States Constitution, and Article I, Sections 5, 9, 10 and 16 of the Ohio Constitution.

***83** The sub-claims raised under this portion include: that Jones's grand jury was improperly constituted because the make-up of the grand jury was based upon race and location within the city; and the process used in Hamilton County to select the foreperson of grand juries that return capital indictments is biased geographically, racially, culturally, and socio-economically. (Petition, Doc. No. 15 at 82.)

7. Mr. Jones's rights under the Fifth, Sixth, Eighth, and Fourteenth Amendments to the United States Constitution, and Article I, Sections 5, 9, 10 and 16 of the Ohio Constitution, and *Batson v. Kentucky*, 476 U.S. 79, 106 S.Ct. 1712, 90 L.Ed.2d 69 (1986) were violated by the discriminatory use of a peremptory challenge by the prosecutor on a prospective juror. Moreover, Mr. Jones was denied a fair and impartial jury because those individuals selected for his venire did not reflect a fair cross section of the community.

8. The trial court erred when it denied Mr. Jones's motion for individual sequestered voir dire in violation of his rights under the Sixth, Eighth and Fourteenth Amendments of the United States Constitution, and Article I, Sections 5, 10, and 14 of the Ohio Constitution.

9. Mr. Jones was denied his right to a fair sentencing determination when the trial judge failed to remove himself as presiding judge over the mitigation hearing in violation of Mr. Jones's rights to due process, fair trial, and freedom from cruel and unusual punishment as guaranteed by the Sixth, Eighth and Fourteenth Amendments of the United States Constitution, Article I, Sections 2, 9, 10 and 16 of the Ohio Constitution.

10. The trial court erred in replacing Juror Geiermann with Juror Brewer prior to Mr. Jones's mitigating hearing.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 167.)

11. The trial court erred in denying Mr. Jones's motion to dismiss the indictment in violation of his rights as guaranteed under the Fifth, Sixth, Eighth, and Fourteenth Amendments of the United States Constitution and Article I, Sections 5, 9, 10, and 14 of the Ohio Constitution.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 167.)

12. The death penalty is imposed in Hamilton County in violation of the Eighth Amendment and Equal Protection Clause because the Hamilton County prosecutor seeks the death penalty in a disproportionate number of cases, compared to the rest of the state.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 167.)

13. The cumulative impact of the appellate ineffectiveness errors violated Mr. Jones's constitutional rights.

Petitioner has withdrawn this sub-claim. (Traverse, Doc. No. 144 at 167.)

For reasons set forth throughout this Report and Recommendation, this claim is without merit in its entirety. The underlying claims were without merit, and

there is not a reasonable probability that the inclusion of these issues on appeal would have changed the result of the appeal. *McFarland v. Yukins,* 356 F.3d 688, 699 (6th Cir.2004), *citing Greer v. Mitchell,* 264 F.3d 663, 676 (6th Cir.2001), *cert. denied,* 535 U.S. 940, 122 S.Ct. 1323, 152 L.Ed.2d 231 (2002). They were not "clearly stronger" than those presented. Appellate counsel was not ineffective.

Eleventh Ground for Relief

***84** Elwood Jones is innocent.

Next Petitioner asserts that he is actually and legally innocent of the offenses for which he has been convicted and sentenced. (Petition, Doc. No. 15 at 85); (Traverse, Doc. No. 144 at 168.) He argues that this is evident in the fact he did not flee the jurisdiction, that there was a significant time delay between the murder and his indictment, and that even the Hamilton County Prosecutor had doubts as to his guilt. (Traverse, Doc. No. 144 at 168.) Respondent states that this claim was not brought on direct appeal, but was brought on post-conviction relief. (Return of Writ, Doc. No. 16 at 43.) The Hamilton County Court of Common Pleas held that the claim was barred by *res judicata. Id.;* (Return of Writ, Doc. No. 16, Apx. Vol. XII at 349 "Findings of Fact, Conclusions of Law, and Entry Dismissing Petition to Vacate.") The court of appeals affirmed the lower court's decision and stated:

> In his twenty-third claim, Jones contends that he is legally innocent. In support of his claim below, he provided his own affidavit in which he stated that he did not kill Nathan, and that his attorneys had told him before trial that the state had offered him a plea bargain, which he refused because he was innocent. He also supplied newspaper articles indicating that Hamilton County sent more people to death row than any other Ohio county and several states.
>
> To the extent that Jones raises a claim of actual legal innocence, the claim fails to constitute a substantive ground for postconviction relief. To the extent, that he is raising issues concerning the manifest weight and sufficiency of the evidence, his claims are barred by *res judicata* in light of the fact that the evidence outside the record fails to materially advance his claim of innocence.

State v. Jones, 2000 WL 1886307 at *5 (Ohio App. 1st Dist.2000).

Absent a showing of cause and prejudice or a demonstration that the Petitioner is "actually innocent," this claim is procedurally defaulted. *Coleman v. Thompson,* 501 U.S. 722, 749, 111 S.Ct. 2546, 115 L.Ed.2d 640 (1991). In applying *Maupin,* there was a state procedural rule in place, to which Petitioner failed to comply. *Maupin v. Smith,* 785 F.2d 135, 138 (6th Cir.1986). This claim was based on the record and should have been presented in direct appeal. Ohio's criminal *res judicata* doctrine is an adequate and independent state ground of decision, actually enforced against Petitioner by the Ohio courts.

To meet the "actual innocence" standard, the petitioner must demonstrate that "it is more likely than not that no reasonable fact finder would have found petitioner guilty beyond a reasonable doubt" or "must show by clear and convincing evidence that, but for a constitutional error, no reasonable juror would have found the petitioner eligible for the death penalty under the applicable state law." *Schlup v. Delo,* 513 U.S. 298, 115 S.Ct. 851, 130 L.Ed.2d 808 (1995); *see also Souter v. Jones,* 395 F.3d 577 (6th Cir.2005). The *Souter* court also held:

> ***85** [I]f a habeas petitioner "presents evidence of innocence so strong that a court cannot have confidence in the outcome of the trial unless the court is also satisfied that the trial was free of nonharmless constitutional error, the petitioner should be allowed to pass through the gateway and argue the merits of his underlying claims." *Schlup v. Delo,* 513 U.S. 298, 316, 115 S.Ct. 851, 130 L.Ed.2d 808 (1995)." Thus, the threshold inquiry is whether "new facts raise[ ] sufficient doubt about [the petitioner's] guilt to undermine confidence in the result of the trial." *Id.* at 317. To establish actual innocence, "a petitioner must show that it is more likely than not that no reasonable juror would have found petitioner guilty beyond a reasonable doubt." *Id.* at 327. The Court has noted that "actual innocence means factual innocence, not mere legal insufficiency." *Bousley v. United States,* 523 U.S. 614, 623, 118 S.Ct. 1604, 140 L.Ed.2d 828 (1998). "To be credible, such a claim requires petitioner to support his allegations of constitutional error with new reliable evidence—whether it be exculpatory scientific evidence, trustworthy eyewitness accounts, or critical physical

> evidence—that was not presented at trial." *Schlup,* 513 U.S. at 324. The Court counseled however, that the actual innocence exception should "remain rare" and "only be applied in the 'extraordinary case.' " *Id.* at 321.

Id. at 590.

In support of his claim, Jones presents the following as new reliable evidence of his innocence: the fact that he was offered a plea agreement by the Hamilton County Prosecutor; the length of time between the murder and his indictment; and the fact he did not flee the jurisdiction. (Traverse, Doc. No. 144 at 168–169.) Jones argues that the Hamilton County Prosecutor had significant doubts as to his guilt and cites to the fact that he was offered a plea bargain agreement on a couple different occasions, including after the jury was sworn. *Id.* at 168. He contends this supports his actual innocence claim as it is a "radical departure" from the patterns and practices of the Hamilton County Prosecutor to offer a plea bargain agreement in an indicted capital case. *Id.* at 168. Additionally he argues the delay in his case is "equally compelling" as he was not indicted until long after the murder and law enforcement had "every piece of evidence they eventually marshaled against him at trial." *Id.* He supports this contention by further stating that this case was handled by experienced law enforcement officials from the start and the delay cannot be blamed on inexperienced officers. *Id.* Finally, in support of his innocence, he counters the State's trial argument that he "was a middle aged, convicted felon who 'knew the ropes.' " by asserting that if he had been guilty he would have fled the jurisdiction, however, he did not flee after the Blue Ash Police Department questioned him, confiscated his personal belongings and car, searched his home and the home of a close friend, and cost him his job at the Embassy Suites. *Id.* at 169.

***86** Respondent counters Petitioner's claim by arguing that it is without merit. (Return of Writ, Doc. No. 16 at 117.) Respondent argues that Jones falls short of demonstrating that given the new evidence it is more likely than not that no reasonable juror would have convicted him and that the "evidence of his innocence is so strong that a court cannot have confidence in the outcome of the trial.' " *Id. citing Lott v. Coyle,* 261 F.3d 594, 602 (6th Cir.2001) *quoting Schlup,* 513 U.S. at 316, 327. Jones has failed to uncover any reliable new evidence of innocence, but rather points to events that happened before trial. *Id.* at 117.

The evidence presented at trial included: the fist-to-mouth injury to Jones's hand; the presence of *eikenella corrodens* in the wound causing an infection; various conflicting stories as to how Jones injured his hard; when asked under oath the "witnesses to the event causing the injury" all denied they had been present at the time of injury; the unique pendant which was found in Jones's toolbox in the trunk of his car; and that the wounds on the victim were consistent with being made by walkie-talkies and the heel of shoes. (Trial Tr. Vol. XIII at 896–898); (Trial Tr. Vol. XIV at 983, 990, 1005, 1041, 1068, 1094, 1111–1112); (Trial Tr. Vol. XV at 1219); (Trial Tr. Vol. XVI at 1392–1394.)

In light of Petitioner's argument and "new evidence" and the evidence presented at trial, that Jones has failed to meet the requirement that "that no juror, acting reasonably, would have voted to find him guilty beyond a reasonable doubt." Evidence of actual innocence used to overcome a procedural default must be "so strong that a court cannot have confidence in the outcome of the trial." *Lott v. Coyle,* 261 F.3d 594, 602 (6th Cir.2001). This is not the case. This claim is without merit.

To the extent Petitioner is claiming actual innocence as a substantive constitutional claim, he fails to state a claim upon which habeas corpus relief can be granted. *Herrera v. Collins,* 506 U.S. 390, 113 S.Ct. 853, 122 L.Ed.2d 203 (1993).

Twelfth Ground for Relief

> The proportionality review that the appellate courts must conduct pursuant to Ohio Rev.Code § 2929.05 is fatally flawed. Therefore, Elwood Jones's death sentence must be vacated pursuant to the Fifth, Eighth, and Fourteenth Amendments to the United States Constitution.

In his Twelfth Ground for Relief, Petitioner makes the argument that the proportionality review of the appellate courts is inadequate in that there is no manner in which to distinguish capital defendants deserving of the death penalty and those who are not. (Petition, Doc. No. 15 at 87.) Petitioner has withdrawn this ground for relief. (Traverse, Doc. No. 144 at 171.)

Thirteenth Ground for Relief

> Elwood Jones's death sentence is constitutionally infirm because Ohio's capital punishment system operates in an arbitrary, capricious, and discriminatory manner in violation of the Fifth, Sixth, Eighth, and Fourteenth Amendments.

***87** In his Thirteenth Ground for Relief, Petitioner asserts that his rights were violated because the Ohio death penalty scheme allows for imposition of the death penalty in an arbitrary and discriminatory manner. (Petition, Doc. No. 15 at 90.) He argues specifically that prosecutors are given uncontrolled discretion and that there is a racial component. *Id.* This ground for relief has been withdrawn. (Traverse, Doc. No. 144 at 171.)

Fourteenth Ground for Relief

> The cumulative effects of the errors and omissions presented in this habeas petition constitute constitutional violations which merit relief.

In his Fourteenth Ground for Relief, Jones asserts that even assuming none of the grounds for relief individually warrant relief, the cumulative effects of the errors and omissions prejudice Jones and violate his constitutional rights. (Petition, Doc. No. 15 at 94); (Traverse, Doc. No. 144 at 171.) Alternatively, the errors, when taken together, are of such magnitude to warrant the granting of a new trial, or at minimum, discovery and an evidentiary hearing. (Traverse, Doc. No. 144 at 171.) He argues this is true because the jurors were permitted to hear many things they should not have heard, and there was evidence they should have heard but did not. *Id.*

Respondent does not allege procedural default, but argues that this claim is without merit. (Return of Writ, Doc. No. 16 at 43, 152.) As none of Jones's claims amount to constitutional violations, then "the 'cumulative effect' of Jones's allegations do not amount to a deprivation of constitutional dimension." *Id.*

In *Lorraine v. Coyle,* 291 F.3d 416 (6th Cir.2002), the court held:

> The Supreme Court has not held that distinct constitutional claims can be cumulated to grant habeas relief. Thus, it cannot be said that the judgment of the Ohio courts is contrary to *Berger,* or to any other Supreme Court decision so as to warrant relief under the AEDPA. *Cf. Walker v. Engle,* 703 F.2d 959, 963 (6th Cir.1983) (pre-AEDPA case; holding that "errors that might not be so prejudicial as to amount to a deprivation of due process when considered alone, may cumulatively produce a trial setting that is fundamentally unfair").

Id. at 447. "We have held that, post-AEDPA, not even constitutional errors that would not individually support habeas relief can be cumulated to support habeas relief." *Moore v. Parker,* 425 F.3d 250, 256 (6th Cir.2005), *citing Scott v. Elo,* 302 F.3d 598, 607 (6th Cir.2002); *Lorraine v. Coyle,* 291 F.3d 416 (6th Cir.2002). Cumulative error claims are not cognizable because the Supreme Court has not spoken on the issue. *Williams v. Anderson,* 460 F.3d 789, 816 (6th Cir.2006), *citing Moore v. Parker,* 425 F.3d 250, 256 (6th Cir.2005).

CONCLUSION

Mr. Jones's Petition for Writ of Habeas Corpus Pursuant to 28 U.S .C. § 2254, (Doc. 15), should be denied. Judgment should be entered in favor of the Respondent and against the Petitioner dismissing the Petition with prejudice.

Appendix

***88** Assignments of Error on direct appeal to the Hamilton County Court of Appeals:

Assignment of Error # 1

> Where trial counsel fails to reasonably investigate the applicable law and facts relevant to plausible actions, to interpose timely objections, to acquaint the court with controlling authority, where available, which would resolve an issue in defendant's favor, and to present effective mitigation, where available, defendant has been deprived of the effective assistance of counsel and a fundamentally fair trial in violation of the Sixth and Fourteenth Amendments to the United States Constitution and the corresponding provisions of the Ohio Constitution, statutes, and laws.

Assignment of Error # 2

Trial tactics and arguments utilized by the prosecutor in the instant case, when considered collectively, deprived defendant of a fair trial and a reliable determination of the appropriate penalty, in violation of the Eighth and Fourteenth Amendments to the United States Constitution and parallel state provisions.

Assignment of Error # 3

The trial court erred to defendant's prejudice when it admitted, over defense objection, evidence that defendant exercised his right to counsel when questioned by police about his alleged involvement in this offense.

Assignment of Error # 4

The trial court erred to defendant's prejudice in allowing Dr. McDonough to introduce the contents of a record which was not prepared by him or in his presence and to offer an expert opinion in a field in which he had no expertise, especially when the opinion was not based on his own knowledge or observations.

Assignment of Error # 5

The trial court erred to defendant's prejudice when it overruled his motion to suppress evidence seized from his vehicle in violation of the Fourth Amendment to the United States Constitution and parallel state constitutional provisions.

Assignment of Error # 6

The trial court erred to the prejudice of defendant in overruling his motion to suppress statements made after his arrest.

Assignment of Error # 7

The trial court erred to defendant's prejudice when it permitted the State to utilize evidence of so-called scientific tests to obtain an indictment, and later a conviction, in violation of defendant's right to the presumption of innocence and to proof beyond a reasonable doubt of every element of the offense as guaranteed by the Due Process Clause of the Fifth Amendment to the United States Constitution and parallel state constitutional provisions.

Assignment of Error # 8

The trial court erred to defendant's prejudice in failing to give an instruction on residual doubt, and in permitting the State to argue that defendant forfeited any right to consideration of a life sentence by failing to present other mitigation.

Assignment of Error # 9

Imposition of the sentence of death on defendant violates his rights under the Eighth Amendment and the Due Process and Equal Protection Clauses of the Fourteenth Amendment of the Federal Constitution, and his right to due course of law and punishment not cruel and unusual under the Ohio Constitution.

Assignment of Error # 10

***89** The trial court erred to defendant's prejudice in accepting the jury's recommendation and sentencing him to death.

Assignment of Error # 11

The trial court erred to defendant's prejudice in recording multiple convictions for murder and submitting them to the jury during the penalty phase, where only one victim was involved.

Assignment of Error # 12

Systemic exclusion of prospective jurors opposed to the death penalty violated defendant's right to a fair and impartial jury which reflects the community from which it is drawn, as guaranteed by the State and Federal Constitutions.

Assignment of Error # 13

The trial court erred to defendant's prejudice in numerous pretrial rulings, in evidentiary rulings, and in accepting and journalizing verdicts of guilty which were not the product of a fair trial, and were not supported by the evidence.

Assignment of Error # 14

The trial court erred to defendant's prejudice when it imposed prison sentences consecutive to the death sentence also imposed.

Assignment of Error # 15

The trial court erred to defendant's prejudice when it gave an instruction on reasonable doubt during the penalty phase which did not meet the constitutional standards imposed on proof for a criminal conviction or sentence.

Assignment of Error # 16

The trial court erred to defendant's prejudice by giving penalty phase jury instructions which relieved the State of its burden of proof and which effectively mandated a death verdict, in violation of Appellant's rights as guaranteed by the Eighth and Fourteenth Amendments to the United States Constitution.

Assignment of Error # 17

The sentence of death imposed on defendant must be vacated because Ohio's death penalty scheme unconstitutionally fails to narrow the field of death eligible defendants in an objective and non-arbitrary fashion.

Assignment of Error # 18

Individual and collective errors mandate reversal of defendant's conviction and sentence.

(Return of Writ, Doc. No. 16, Apx. Vol. III at 37–73.)

Propositions of Law pled in the Ohio Supreme Court:

Proposition of Law # 1

Defense counsel's failure to object to the damaging testimony of defendant's physician on the grounds that it revealed material that was protected by the doctor-patient privilege deprived defendant of the effective assistance of counsel, and a fundamentally fair trial, in violation to the Sixth and Fourteenth Amendments to the United States Constitution and the corresponding provisions of the Ohio Constitution, statutes and rules.

Proposition of Law # 2

Defendant was denied effective assistance when counsel failed to interpose a specific objection to the admission of statements allegedly made after he invoked his right to silence and to counsel, when those statements were deliberately elicited by the police, and to cite the court to controlling authority to support suppression.

Proposition of Law # 3

***90** Failure to conduct adequate voir dire to insure that defendant does not face a jury predisposed to both conviction and imposition of the death penalty constitutes ineffective assistance of counsel.

Proposition of Law # 4

Failure to present available mitigation evidence constitutes ineffective assistance of counsel.

Proposition of Law # 5

Where the prosecutor's actions, individually and collectively, act to undermine the fairness of the trial proceedings, such actions deny defendant due process of law, a fair trial and a reliable determination of the appropriate penalty, in violation of the Eighth and Fourteenth Amendments to the United States Constitution and parallel state provisions.

Proposition of Law # 6

A trial court may not allow the prosecutor to use facts not in evidence to appeal to the passions and prejudices of the jury in violation of the accused's rights under the Sixth and Fourteenth amendments to the United States Constitution and his concomitant rights under Article I Section 10 of the Ohio Constitution.

Proposition of Law # 7

A prosecutor may not denigrate the role and trial tactics of defense counsel nor suggest that defense counsel is attempting to hide the truth or improperly influence the jury to violate its oath.

Proposition of Law # 8

Consideration of the nature and circumstances of the offense can only be considered as aggravating factors, coupled with appeals to emotion and prejudice, violates Ohio's death penalty statute and defendant's right to be free from arbitrary infliction of the death penalty as guaranteed by the Eighth Amendment to the United States Constitution, and parallel state provisions.

Proposition of Law # 9

Defendant's request for counsel is not probative evidence of guilt, and the introduction of such evidence over defendant's objection can only be interpreted as an attempt to violate his Fifth Amendment rights by

suggesting to the jury that a request for counsel can be used against him.

Proposition of Law # 10

An expert may not introduce the contents of a record which was not prepared by him or in his presence and to offer an expert opinion in a field in which he had no expertise, especially when the opinion was not based on his own knowledge or observations.

Proposition of Law # 11

Evidence seized from defendant's vehicle should have been suppressed when the affidavit in support of the search warrant for defendant's car contained material misstatements of fact, which rendered the entire warrant invalid, and any search conducted pursuant to it a violation of the Fourth Amendment to the United States Constitution and parallel state constitutional provisions.

Proposition of Law # 12

The admission into evidence of the statements elicited from defendant while in custody after he requested, but was not provided counsel, violates the Fifth, Sixth and Fourteenth Amendments of the United State Constitution and parallel constitutional and statutory provisions of the State of Ohio.

Proposition of Law # 13

***91** Testimony offered as expert opinion concerning the relationship between wounds on the victim's body and objects which might have caused them, did not meet the criteria for admission of expert testimony, and was highly prejudicial to defendant in violation of his right to the presumption of innocence and to proof beyond a reasonable doubt of every element of the offense as guaranteed by the Due Process Clause of the Fifth Amendment to the United States Constitution and parallel state constitutional provisions.

Proposition of Law # 14

Failure to instruct the jury on residual doubt becomes error when the State is permitted to argue that defendant has forfeited any right to a weighing of aggravating and mitigating factors by presenting no other mitigation, and the jury is repeatedly told that their verdict is only a recommendation.

Proposition of Law # 15

Imposition of the sentence of death on defendant violates his rights under the Eighth Amendment and the Due Process and Equal Protection Clauses of the Fourteenth Amendment of the Federal Constitution, and his right to due course of law and punishment not cruel and unusual under the Ohio Constitution.

Proposition of Law # 16

Defendant's sentence violates the Eighth and Fourteenth Amendments to the Constitution of the United States, and parallel state provisions, because it is disproportionately severe in relation to the crime committed, and to sentences visited upon others for the same crime in the same and other jurisdictions.

Proposition of Law # 17

Defendant's death sentence must be set aside because it is disproportionately severe when compared to other cases in Hamilton County and in the State of Ohio in which capital sentencing decisions were made.

Proposition of Law # 18

Although multiple charges of aggravated murder may be submitted to the jury during the guilt phase of trial, where there is only one death charge there can be only one conviction, and presentation to the jury of multiple counts, with multiple specifications, followed by imposition of multiple death sentences, violates defendant's right to be free from cruel and unusual punishment under the State and Federal Constitutions.

Proposition of Law # 19

Systematic exclusion of prospective jurors opposed to the death penalty violated defendant's right to a fair and impartial jury which reflects the community from which it is drawn, as guaranteed by the State and Federal Constitutions.

Proposition of Law # 20

Exclusion of those opposed to the death penalty results in a jury biased in favor of guilt, and of death, denying defendant due process, equal protection and a fair and impartial jury.

Proposition of Law # 21

The judgments rendered against defendant by the trial court must be reversed because they were the product of collective consideration of admissible and inadmissible evidence, because the evidence presented was insufficient, as a matter of law, to support the verdicts, and because errors by the court, defense counsel and the prosecution combined to deny defendant a fair trial in violation of the Fourteenth Amendment to the Federal Constitution, corresponding provisions of the Ohio Constitution, and the laws and evidentiary rules of the State of Ohio.

Proposition of Law # 22

***92** A term of imprisonment can be made consecutive only to another term of imprisonment, therefore, a trial court cannot legally impose a term of imprisonment to be served consecutively to a sentence of death.

Proposition of Law # 23

Ohio's statutory definition of reasonable doubt allows a jury to return convictions based on a degree of proof which fails to meet the constitutional guarantee of due process of law embodied in the Fourteenth Amendment to the United States Constitution and corresponding language in the Ohio Constitution.

Proposition of Law # 24

An instruction which mandates a death recommendation if the jury is firmly convinced of the truth of the charge, and which lessens the burden of proof on the State, is constitutionally infirm.

Proposition of Law # 25

The statutorily mandated proportionality review currently being employed in Ohio does not comport with the requirements of the Fifth, Eighth and Fourteenth Amendments to the United States Constitution, Article One, Sections 10 and 16 of the Ohio Constitution, or the plain language of O.R.C. § 2929.05.

Proposition of Law # 26

Individual and collective errors, whether raised by appellate counsel or not, mandate reversal of defendant's conviction and sentence.
(Return of Writ, Doc. No. 16, Apx. Vol. IV at 16–111.)

Claims for Relief pled in Petitioner's petition for post-conviction relief under Ohio Revised Code § 2953.21

First Ground for Relief

Petitioner Jones' conviction and sentence are void or voidable because Hamilton County seeks to overprosecute death cases, which results in an arbitrary, unreasoning and capricious imposition of the death penalty.

Second Ground for Relief

Petitioner Jones' conviction and sentence are void or voidable because Hamilton County underrepresents minorities in their grand juries. The jury selection process utilized in Hamilton County results in petit and grand juries that are biased geographically, racially, culturally, and socio-economically.

Third Ground for Relief

Petitioner Jones' conviction and sentence are void or voidable because the process utilized in Hamilton County to select the foremen of grand juries that return capital indictments is biased geographically, racially, culturally, and socio-economically.

Fourth Ground for Relief

Petitioner Jones' conviction and/or sentence are void or voidable because the systematic exclusion of African–Americans from his prospective petit jury panel violated his rights as guaranteed by the Fifth, Sixth, Eighth and Fourteenth Amendments of the United States Constitution, and Article I, Sections 2, 5, 9, and 10 of the Ohio Constitution.

Fifth Ground for Relief

Petitioner Jones' conviction and/or sentence are void or voidable because the use of peremptory challenges in a racially discriminatory manner during voir dire violated his rights as guaranteed by the Fifth, Sixth, Eighth and Fourteenth Amendments of the United States Constitution, and Article I, Sections 2, 5, 9, and 10 of the Ohio Constitution.

Sixth Ground for Relief

***93** Petitioner Jones' convictions and sentences are void and/or voidable because he was denied effective

assistance of counsel during the trial phase of his capital trial as guaranteed by the Sixth and Fourteenth Amendments to the United States Constitution and Section 10, Article I of the Ohio Constitution, C.P. Sup. R. 20(IV)(D). *Strickland v. Washington,* 466 U.S. 669 (1984); *Glenn v. Tate,* 71 F.3d 1204 (6th Cir.1995).

Seventh Ground for Relief

Petitioner's conviction and death sentences are void or voidable because his counsel abdicated their duty to investigate. Absent investigation and preparation, trial counsel were ineffective for failing to exercise Petitioner's right to confront state witness Dr. McDonough. In addition, Petitioner's counsel rendered ineffective assistance of counsel by failing to properly utilize Dr. Solomkin as a defense witness. *Strickland v. Washington,* 466 U.S. 688 (1984); *Kentucky v. Stincer,* 482 U.S. 730, 107 S.Ct. 2658, 96 L.Ed.2d 631 (1987); *Davis v. Alaska,* 415 U.S. 306 (1974).

Eighth Ground for Relief

Petitioner's conviction and death sentence are void or voidable because the prosecutor concealed evidence favorable to Mr. Jones and material to guilt and punishment.

Ninth Ground for Relief

Petitioner's conviction and death sentence are void or voidable because his counsel were rendered ineffective when the prosecutor concealed evidence favorable to Mr. Jones and material to guilt and punishment. Moreover, independent of the prosecution's act and omissions, Petitioner's trial counsel were ineffective in their own right for failing to conduct an adequate investigation which should have included the rudimentary task of thoroughly inspecting all of the State's physical evidence and any records pertaining to that evidence.

Tenth Ground for Relief

Petitioner Jones' conviction and/or sentence are void or voidable because he was denied the effective assistance of counsel in the trial phase of his capital trial as guaranteed by the Fifth, Sixth and Fourteenth Amendments of the United States Constitution, Sections 10 and 16, Article I of the Ohio Constitution, and *Strickland v. Washington,* 466 U.S. 668, 686, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984).

Eleventh Ground for Relief

Petitioner Jones' convictions and/or sentences are void or voidable because he was denied the effective assistance of counsel in the trial phase of his capital trial as guaranteed by the Fifth, Sixth and Fourteenth Amendments of the United States Constitution, Sections 10 and 16, Article I of the Ohio Constitution, and *Strickland v. Washington,* 466 U.S. 668, 686, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984).

Twelfth Ground for Relief

Petitioner Jones' convictions and sentences are voidable because at Petitioner's trial the trial court refused to allow the testimony of a witness regarding facts pertinent to Petitioner Jones's indictment and prosecution for capital murder. The trial court's refusal deprived Elwood Jones, Jr. of his right to present a defense at his capital trial in violation of his rights to compulsory process and to due process in violation of the Sixth and Fourteenth Amendments to the United States Constitution and §§ 1, 2, 5, 9, 10, 20 of Art. I of the Ohio Constitution. The trial court's action prejudiced Mr. Jones.

Thirteenth Ground for Relief

***94** Petitioner Jones' convictions and/or sentences are void or voidable because he was denied effective assistance of counsel during the course of his trial as guaranteed by the Fifth, Sixth and Fourteenth Amendments to the United States Constitution and Section 10, Article I of the Ohio Constitution, C.P. Sup. R. 20(IV)(D). *Strickland v. Washington,* 466 U.S. 668, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984); *Glenn v. Tate,* 71 F.3d 1204 (6th Cir.1995).

Fourteenth Ground for Relief

Petitioner's conviction and death sentence are void or voidable because his counsel were constitutionally ineffective when they informed the jury of Petitioner's prior criminal record and when they failed to object when the prosecutor did the same. No reasonable defense trial strategy could possibly explain this conduct. Petitioner himself never had any conversations with his trial counsel concerning whether his counsel

should inform and/or permit others to inform the jurors of his past criminal record, but he adamantly opposed such a notion. When he objected to his own counsel informing the jurors of his criminal record, Petitioner was rebuffed by them with the threat that the trial court would have him bound and gagged if he did not remain quiet at counsel table.

Fifteenth Ground for Relief

Petitioner's conviction and death sentence are void or voidable because his counsel were constitutionally ineffective when they failed to object to unlawful and unconstitutional jury instructions. There can not be and there is not any objectively reasonable tactic basis for Petitioner's trial counsel's failure to raise these objections. Moreover, reasonably competent capital defense trial counsel would have- and Petitioner's trial counsel should haverequest [sic] jury instructions that complied with the constitutional, legal, statutory and procedural requirements that underlie the constitutional counterparts to the defective instructions that Petitioner's counsel failed to raise during his trial.

Sixteenth Ground for Relief

The record of Petitioner's trial contains much evidence regarding a certain pair of brown shoes. The prosecution wanted to connect these shoes to Petitioner in order to link them with certain forensic testimony that the prosecution believed tied the shoes to the bruise patterns on the decedent's body. Although the shoes were found in the home of his friend Earlene Metcalff, they were not his shoes. Petitioner made it clear to his trial counsel that these shoes were not his shoes. Nonetheless, Petitioner's counsel stipulated the Petitioner's ownership of these shoes over Petitioner's express objection voiced to his counsel. By so doing, Petitioner's trial counsel violated Petitioner's right to effective assistance of counsel, his right to confront the state's case, his right to due process and his right to a fair trial. U.S. Const., amends. V, VI, VIII, IX, XIV; Ohio Const., art. I, §§ 1, 2, 5, 9, 10, 16 and 20.

Seventeenth Ground for Relief

***95** Petitioner Jones' conviction and/or sentences are void or voidable because he was denied effective assistance of counsel during the course of his trial as guaranteed by the Fifth, Sixth and Fourteenth Amendments to the United States Constitution and Section 10, Article I of the Ohio Constitution, C.P. Sup. R. 20(IV)(D). *Strickland v. Washington,* 466 U.S. 668, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984); *Glenn v. Tate,* 71 F.3d 1204 (6th Cir.1995).

Eighteenth Ground for Relief

The judgment and sentence against Mr. Jones are void or voidable because he did not receive the effective assistance of counsel during the mitigation phase of his trial. Counsel fell below a minimum standard of reasonable legal representation by failing to effectively investigate, identify and present to Mr. Jones available mitigation evidence. Whether or not Mr. Jones or any other person facing a capital indictment eventually waives the presentation of mitigation, his counsel has an independent obligation to fully investigation [sic] mitigation evidence. Only after a person stands convicted and actually faces the life or death decision to waive or present mitigation evidence can that person make a knowing, intelligent and voluntary waiver of the right to present mitigation. And it is impossible to make such a knowing, intelligent and voluntary waiver unless defense counsel has fully investigated mitigation, presents that available mitigation evidence to the defendant in detail, and counsels the defendant about the full factual and legal ramifications of this life or death decision.

Nineteenth Ground for Relief

Petitioner Jones' convictions and/or sentences are void or voidable because he was denied the effective assistance of counsel in the trial phase of his capital trial as guaranteed by the Fifth, Sixth and Fourteenth Amendments of the United States Constitution, Sections 10 and 16, Article I of the Ohio Constitution, and *Strickland v. Washington,* 466 U.S. 668, 686, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984).

Twentieth Ground for Relief

Petitioner Jones' conviction and/or sentence are void or voidable because he was denied the effective assistance of counsel in the trial phase of his capital trial as guaranteed by the Fifth, Sixth, Eighth, Ninth and Fourteenth Amendments of the United States Constitution and Sections 10 and 16, Article I of the Ohio Constitution. *Strickland v. Washington,* 466 U.S. 668, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984).

Twenty–First Ground for Relief

Petitioner Jones' conviction and/or sentence are void or voidable because he was denied the effective assistance of counsel in the trial phase of his capital trial as guaranteed by the Fifth, Sixth, Eighth, Ninth, and Fourteenth Amendments of the United States Constitution and Sections 10 and 16, Article I of the Ohio Constitution. *Strickland v. Washington,* 466 U.S. 668, 104 S.Ct. 2052, 80 L.Ed.2d 674 (1984).

Twenty–Second Ground for Relief

Petitioner Jones' convictions and/or sentences are void or voidable because the juror misconduct that occurred during his capital sentencing hearing denied him a fair and impartial determination of his sentence in violation of the Fifth, Sixth, Eighth, and Fourteenth Amendments to the Constitution of the United States and Article I, Sections 1, 2, 5, 9, 10, 16 and 20 of the Ohio Constitution.

Twenty–Third Ground for Relief

***96** Petitioner is actually and legally innocent of the offenses for which he has been convicted, sentenced to death and sent to death row. For all of the reasons recited in this post-conviction petition, on his direct appeal of right, and in his application for reopening of his appeal, it is evident that Elwood Jones is at least legally innocent.

Twenty–Fourth Ground for Relief

Petitioner Jones' conviction and sentence are void or voidable because the post-conviction process provides an inadequate corrective process.

Twenty–Fifth Ground for Relief

The judgment and sentence against Mr. Jones are void or voidable because Ohio Rule of Criminal Procedure 35(A) unconstitutionally restricts the presentation of a death-sentenced Petitioner's claims. Rule 35(A) enforces a three-page per claim pleading limitation which further renders Ohio's putative post-conviction meaningless.

Twenty–Sixth Ground for Relief

Petitioner Jones' convictions and/or sentences are void or voidable because the death penalty is disproportionately meted out to those defendants who are racial minorities and/or those defendants who are accused of killing white victims. This disparity exists in Hamilton County, the State of Ohio, and in all of the thirty-seven (37) states in the United States that have provisions for capital punishment.

Twenty–Seventh Ground for Relief

The judgment and sentence against Mr. Jones are void or voidable because the death penalty, as administered in the State of Ohio, violates his constitutional right to protection from cruel and usual [sic] punishment as guaranteed by the Eighth Amendment and the due process clause and equal protection clause of the United States Constitution, and Article I, Sections 2, 9, and 16 of the Ohio Constitution.

Twenty–Eighth Ground for Relief

The judgment and sentence against Mr. Jones are void or voidable because the death penalty, as administered in the State of Ohio, violates his constitutional right to protection from cruel and unusual punishment as guaranteed by the Eighth Amendment and the due process clause and equal protection clause of the United States Constitutions, and Article I, Sections 2, 9, and 16 of the Ohio Constitution.

Twenty–Ninth Ground for Relief

Petitioner Jones' judgment and sentence are void or voidable because, assuming *arguendo* that none of the Grounds for Relief in his Post–Conviction Petition individually warrant the relief sought from this court, the cumulative effects of the errors and omissions as presented in the Petition in paragraphs one (1) through two hundred eleven (211) have been prejudicial to the Petitioner and have denied the Petitioner his rights as secured by the Fourth, Fifth, Sixth, Eighth and Fourteenth Amendments to the United States Constitution and Article I, Sections 2, 9, 10, and 16 of the Ohio Constitution.
(Return of Writ, Doc. No. 16, Apx. Vol. V at 6–75.)

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